Specification

A novel 2-pyridinecarboxamide derivative.

The Field of Technology

This invention relates to the following, namely, the glucokinase activator which is containing as effective ingredient pyridine-2-carboxamide derivative. Moreover, it is related to a novel 2-pyridinecarboxamide derivatives or salts thereof.

Background Technique

Glucokinase (GK) (ATP : D-hexose 6-phosphotransferase, EC2.7.1.1) is one of four kinds of mammalian hexokinases (hexokinase IV). Hexokinase is an enzyme that catalyses the reaction of the first stage of the glycolytic pathway from glucose to glucose 6 phosphate. Glucokinase expression is mainly localised in liver and pancreatic β cells, and by controlling the rate-limiting step of glucose metabolism in these cells it has an important role in glucose metabolism of the whole body. The glucokinase of liver and pancreatic β cells have respectively different sequences of the N terminal 15 amino acids due to different splicing, but their enzymatic characteristics are the same. In the three hexokinases (I, II, III) other than the glucokinase, the enzyme activity is saturated at glucose concentration of 0.1 mM or less, whereas, the Km with respect to glucose of glucokinase is at 8 mM which is close to the physiological blood glucose level. Accordingly, facilitation of intracellular glucose metabolism occurs via glucokinase in response to the blood glucose change from the normal blood sugar (5 mM) to postprandial blood glucose rise (10-15 mM).

About 10 years ago, a hypothesis was proposed that the glucokinase works as a glucose sensor in pancreatic β cells and liver (for example Garfinkel D et al, 'Computer modeling identifies glucokinase as glucose sensor of Pancreatic β-cells', American Journal Physiology, Vol 247, (3Pt2) 1984, pp. 527-536). In practice, it is clear from results of a recent glucokinase genetically modified mouse, that glucokinase, carries out an important role in glucose homeostasis of whole body. The mouse whose glucokinase gene is destroyed dies soon after birth (Grupe A et al., 'Transgenic Knockouts reveal a critical requirement for pancreatic β cell glucokinase in maintaining glucose homeostasis', Cell, Vol 83, 1995, p69-78), while on the other hand, for normal and diabetes mellitus mice which overexpressed glucokinase, the blood glucose level becomes low (Ferre T et al. 'Correction of diabetic alterations by glucokinase', Proceedings of the National Academy of Sciences of the U.S.A, vol 93, 1996, p7225-7230). Although the reaction of hepatocytes is different from pancreatic β cells when glucose concentration rises, but both cells correspond in the direction to lower the blood glucose. Pancreatic β cells start to secrete more insulin, the liver takes up more glucose and stores it as glycogen, and at the

same time, decreases the sugar release.

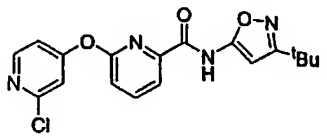
In this way fluctuation of glucokinase enzyme activity is carrying out important role in glucose homeostasis of mammal through liver and pancreas β cells. A mutation of glucokinase gene has been discovered in the cases of diabetes mellitus that occurs in youth, known as MODY2 (maturity-onset diabetes of the young), and the reduction of glucokinase activity causes a blood glucose rise (Vionnet N et al., 'Nonsense mutation in the glucokinase gene cause early-onset non-Insulin-dependent diabetes mellitus' Nature Genetics, Vol 356, 1992 pp. 721-722). On the other hand, the lineage having mutation which causes an increase in glucokinase activity is also found, and such persons show hypoglycemic symptoms (Glaser B, 'Familial hyperinsulinism caused by an activating glucokinase mutation', New England Journal Medicine, Vol 338, 1998, pp. 226-230).

From these, glucokinase also plays an important role in glucose homeostasis in humans, by acting as a glucose sensor. On the other hand, blood glucose regulation using glucokinase sensor system is regarded as possible in many type II diabetics. Because insulin secretion promotion action of pancreatic β cells and enhanced sugar uptake and sugar release suppression action in liver are expected, it is regarded as useful as therapeutic drug of type II diabetes.

Recently, it has been discovered that pancreas β cell type glucokinase was expressed in rat brain, especially localised in the feeding centre (Ventromedial hypothalamus, VMH). About 20 % of the neurons of VMH, called glucose responsive neurons, has been considered in the prior art as having an important role in body weight control. Overeating occurs when glucose metabolism is suppressed by glucose analogue glucosamine intracerebral administration, in contract to the reduction of food intake when glucose is administered to rat brain. From electrophysiological experiments, it is observed that glucose responsive neurons are activated in response to physiological glucose concentration change (5-20 mM), but activity is suppressed when glucose metabolism is inhibited with glucosamine and the like. It is assumed that the mechanism in glucose concentration sensitive system of VHM is through glucokinase as it is for insulin secretion of pancreatic β cells. Accordingly, there is a possibility that the substances which can activate glucokinase of VHM in addition to liver and pancreatic β cells can correct the problem of obesity in many type II diabetics in addition to blood glucose correction effect.

From the aforesaid description, the compound which has glucokinase activation action is useful as therapeutic agent and/or preventive agent of diabetes, or therapeutic agent and/or preventive agent of chronic complication of diabetes mellitus such as retinopathy, nephropathy, neuropathy, ischemic heart disease, arteriosclerosis or the like, further as therapeutic agent and/or preventive agent of obesity.

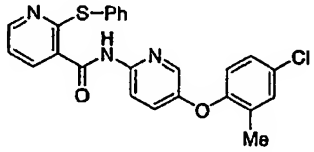
As the compound having the pyridine skeleton of compound (I) in accordance with this invention and the compound having amide group bonded to aforesaid pyridine skeleton, the compound represented by following constitutional formula (IV) is described (Kokai 5-213382).



(IV)

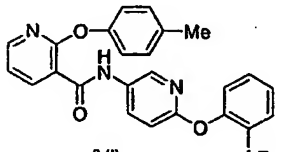
However, the positional relation of amide bond and C=N of the isoxazole group of compound (IV) described in Kokai 5-213382 is different from the positional relation of amide bond and C=N of the compound in accordance with this invention, and it is also different in the point that applications of the compound in accordance with this invention is diabetes mellitus but applications of Kokai 5-213382 is herbicide.

Moreover, as the compounds which are structurally similar, and also have applications of diabetes mellitus, the compounds represented by the following formula (V)



(V)

or the following formula (VI)



(VI)

are described (Kokai 2001-522834).

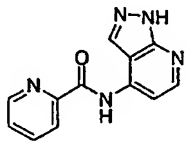
Diabetes mellitus is described as one of applications of the compound described in Kokai 2001-522834 and it is common to applications of compound (I) in accordance with this invention.

Moreover, compound (V) or (VI) described in Kokai 2001-522834 is common to the compound (1) in accordance with this invention in the point of having pyridine skeleton as basic skeleton and also having amide bond on the aforesaid pyridine ring.

However, it is different in the point that the compound (1) in accordance with this invention has substituent on 6 position of the pyridine ring, but the aforesaid compound (V) or (VI) does not have substituent on 6 position of the pyridine ring.

Moreover, the compound (1) in accordance with this invention has amide bond adjacent to the nitrogen atom constructing pyridine ring, on the other hand, the compound (VI) described in Kokai 2001-522834 has amide bond at the position one carbon away from the nitrogen atom substituting the pyridine ring, and the relative positional relation of C=N part constructing the pyridine ring which is the part corresponding to B ring in accordance with this invention and the amide bond is different between the compound (I) in accordance with this invention and the compound (VI) in accordance with Kokai 2001-522834.

Moreover, as the compound having pyridine-2-carboxamide skeleton in the same way as in compound (I) in accordance with this invention, the compound represented by formula (VII)



(VII)

is described (WO 01/81345). However, the relative positional relation of nitrogen atom in 1H-pyrazolo [3,4-b] pyridin-4-yl group which is bonded to nitrogen atom of amide bond described in compound (VII) and the amide bond is different from the relative positional relation of C=N in B ring of compound (I) in accordance with this invention and the amide bond. Moreover, it is different in the point that hydrogen atom is bonded in the 3 and 6 positions of pyridine skeleton of formula (VII), but in the compound (I) in accordance with this invention, the groups other than hydrogen atom are bonded, and therefore formula (VII) and compound (1) in accordance with this invention are different to each other as the whole structure.

Accordingly although the compound described in WO 01/81345 is common to the compound (1) in

accordance with this invention in the point of having basic skeleton, pyridine-2-carboxamide, it is different from the compound in accordance with this invention in the form of substituent bonded to the pyridine skeleton, and has a different structure from the compound of this invention.

Problems to be overcome by this invention is to put forward a therapeutic agent and/or preventive agent of diabetes in which glucokinase activity is increased by bonding to glucokinase, and moreover, to put forward an anti-obesity agent acting by stimulating satiety center by activating glucokinase.

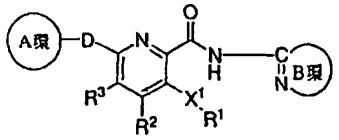
There are advantages, as described above, that the compounds in accordance with this invention have drug efficacy superior to preexisting diabetes mellitus, and the development of new drug efficacy which was not present in preexisting diabetes mellitus drug is possible or the like.

Therefore, these inventors carried out assiduous investigation to develop the novel diabetes mellitus drugs having drug efficacy superior to preexisting diabetes mellitus drug by the action different from aforesaid existing agent and also having a new drug efficacy. As a result, they discovered that the compound represented by formula (I) had glucokinase activation action. This invention was completed based on this discovery.

Disclosure of the Invention

This invention relates to

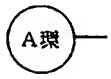
1. A compound represented by formula (I) or pharmacologically acceptable salts thereof

ring A  ring B

(I)

[wherein, X1 denotes N, S or O, or divalent saturated hydrocarbon group of carbon number 1-6 (when carbon number of said divalent saturated hydrocarbon group is 2 or more, one of carbon atom in said divalent saturated hydrocarbon group may be substituted by nitrogen atom, oxygen atom or sulfur atom), R1 denotes 6-10 membered aryl group, 5-10 membered heteroaryl group, cycloalkyl group of carbon number 3-7 or lower alkyl group {the said R1 may have, on R1, one or two groups selected from the group comprising amino group, lower alkyl group (hydrogen atom of lower alkyl group may be substituted by hydroxy group, lower alkoxy group, halogen atom, carbamoyl group, mono or di-lower alkyl carbamoyl group, carboxyl group, alkoxy carbonyl group, alkanoyl group, amino group or mono or di-lower alkyl amino group), lower alkoxy group (hydrogen atom of methyl group or

methylene group composing said lower alkoxy group may be substituted by hydroxy group, halogen atom, carbamoyl group, mono or di-lower alkyl carbamoyl group, carboxyl group, alkoxycarbonyl group, alkanoyl group, amino group or mono or di-lower alkyl amino group), carbamoyl group, lower alkyl carbamoyl group, dilower alkyl carbamoyl group, carbamoyl amino group, carbamoyloxy group, carboxyl group, cyano group, sulphamoyl group, trifluoromethyl groiup, halogen atom, hydroxy group, formyl group, C2-C6-alkanoyl group, N-C2-C6-alkanoyl amino group, C1-C6-alkylthio group, N-C1-C6-alkyl sulphamoyl group, N,N-di-C1-C6-alkyl sulphamoyl group, C1-C6-alkyl sulphinyl group, C1-C6-alkylsulfonyl group, N-C1-C6-alkylsulfonyl amino group, C1-C6-alkoxycarbonyl group, N-C1-6 alkylamino group and N,N-di-C1-C6-alkylamino group}, D denotes O or S, R2 and R3 may be the same or different and denote hydrogen atom, lower alkyl group, lower alkoxy group, halogen atom, formula (II)

ring A 

(II)

shows 5-7 membered heteroaryl group or 6-10 membered aryl group which may have on the said ring, 1 or 2 group selected from the group comprising lower alkyl group, lower alkoxy group, trifluoromethyl group, hydroxy group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group) and halogen atom, and formula (III)

ring B

(III)

shows monocyclic or polycyclic heteroaryl group wherein carbon atom in the said ring bonded to nitrogen atom of the amide group contained in formula (1) forms C=N with nitrogen atom in the said ring {the said heteroaryl group may have in B ring, 1 or 2 substituent selected from the group comprising lower alkyl group, lower alkoxy group, halogen atom, trifluoromethyl group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group), amino (the said amino group may be substituted by lower alkyl group), alkanoyl group, carboxyl group, alkoxycarbonyl group and cyano group}].

2. A compound in accordance with aforesaid 1, wherein D is S.

3. A compound in accordance with any of aforesaid 1 or 2, wherein R2 and R3 are both hydrogen atoms.

4. A compound in accordance with any of aforesaid 1-3, wherein A ring is phenyl group, isothiazolyl group, imidazolyl group, oxazolyl group, thiadiazolyl group, thienyl group, triazolyl group, tetrazolyl group, pyridyl group, pyrimidinyl group, furyl group, thiazolyl group, isoxazolyl group or pyrazolyl group that which may have 1 or 2 group selected from the group comprising lower alkyl group, lower alkoxy group, trifluoromethyl group, hydroxy group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group) and halogen atom on the said ring.

5. A compound in accordance with any of aforesaid 1-4, wherein X1 is a group selected from the group comprising nitrogen atom, sulfur atom, oxygen atom, -CH2-, -N-CH2-, -S-CH2-, -O-CH2-, -CH2-N-, -CH2-O- and -CH2-S-.

6. A compound in accordance with any of aforesaid 1-5, wherein B ring is 5-6 membered heteroaryl group having at least one nitrogen atom of C=N composing said ring as heteroatom of said ring or 9-10 membered heteroaryl group in which said heteroaryl group and phenyl group or pyridyl group are condensed.

7. A compound in accordance with any of aforesaid 1 to 6, wherein R1 is 6-10 membered aryl group, 5-10 membered heteroaryl group or cycloalkyl group of carbon number 3-7.

8. A compound in accordance with any of aforesaid 1 to 6, wherein R1 is 6-10 membered aryl group or 5-10 membered heteroaryl group.

9. A compound in accordance with any of aforesaid 1-6, wherein R1 is 6-10 membered aryl group.

10. A compound in accordance with any of aforesaid 1-6, wherein R1 is 5-10 membered heteroaryl group.

11. A compound in accordance with aforesaid 9 or 10, wherein substituent of A ring is hydrogen atom, lower alkyl group, lower alkoxy group, hydroxy group or hydroxy lower alkyl group (hydrogen atom of hydroxy group in hydroxy lower alkyl group may be further substituted by lower alkyl group).

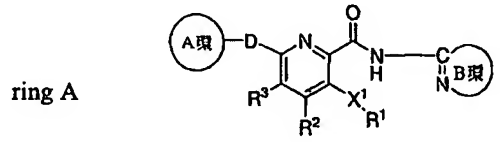
12. A compound in accordance with any of aforesaid 9 to 11, wherein B ring is thiazolyl group, imidazolyl group, isothiazolyl group, thiadiazolyl group, triazolyl group, oxazolyl group, isoxazolyl

group, pyrazinyl group, pyridyl group, pyridazinyl group, pyrazolyl group, pyrimidinyl group, pyrido thiazolyl group or benzothiazolyl group.

13. A compound in accordance with any of aforesaid 1-10, wherein substituent of B ring is hydrogen atom, lower alkyl group, halogen atom, hydroxyalkyl group, amino alkyl group or alkanoyl group.

14. A compound in accordance with any of aforesaid 9 to 12, wherein substituent of R1 is hydrogen atom, hydroxyalkyl group, lower alkyl group, lower alkoxy group, carbamoyl group, alkylcarbamoyl group, dialkyl carbamoyl group, cyano group, trifluoromethyl group, halogen atom, 2-6C alkanoyl group, N-C2-C6 alkanoyl amino group, C1-C6- alkylsulfonyl group, C1-C6- alkylamino group or amino alkyl group.

15. A compound or pharmacologically acceptable salts thereof, wherein the compound represented by aforesaid formula (I)



(I)

(in the formula, each symbol has the same aforesaid definitions) is

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-imidazol-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(thiazol-2-yl-sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(2-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-phenyl sulphanyl-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyloxy)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenylmethyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(3-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(2,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-cyano-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-4-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-acetyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(thiophen-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-chloro-phenyl sulphanyl)-6-(4H-[1,2,41 triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(3H-[1,2,3] triazol-4-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methylsulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazole-3-yl-sulphanyl)-N-(5-hydroxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methoxymethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-trifluoromethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-dimethylamino methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2- pyridine carboxamide,

3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methyl sulphamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-hydroxy-cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridazine-3-yl)-2-pyridine carboxamide,

3-(pyrazine-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(1-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4) triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-phenoxy-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(2-chloro-phenylmethyl-amino)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis (pyridine-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(4-fluoro-phenyl sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(thiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(5-methyl-[1,3,4] thiadiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,3,4] thiadiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl carbonyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrimidine-4-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-ethoxycarbonyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-phenyloxy methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazole-2 yl)-2-pyridine carboxamide,

3-phenyl sulphanyl methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-phenylmethyl-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro- phenyl methyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminomethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-4-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(4-hydroxyethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methoxycarbonyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(pyrimidine-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(1-methyl-pyrrolidine-3-yloxy)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-diethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-pyrrolidino ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-dimethylaminoethyl oxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyrazol-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-carbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(5-bromo-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,5] thiadiazol-3-yl)-2-pyridine carboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methoxy-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-[3-cyclopropyl-[1,2,4]-thiadiazol-5-yl]-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2-fluoro-pyridin-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(2-methoxy-pyrimidin-5-yl sulphanyl)-6-(2H-[1,2,41 triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-diethylcarbamoyl methyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-cyclopropyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(pyrazol-4-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylamino sulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(5-fluoro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazine-3-yl)-2-pyridine carboxamide,

3-(4-carboxy-phenyl sulphanyl)-6-(5-methyl-[1,2,4] triazole-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [4,5-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(5-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4,4-difluoromethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-hydroxyethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(2-methyl-imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-hydroxymethyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl)-phenyl sulphanyl]-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-methyl-1H-indazol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(3-methyl-[1,2,4]-triazolo-[4,3-a]-pyridin-7-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(1H-imidazol-1-yl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4,5-dimethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4,5-dimethyl-4H-[112,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-(1-methoxyethyl)-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-hydroxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-trifluoromethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-trifluoromethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(3-fluoro-4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-[4-(1,1-dimethyl-1-hydroxymethyl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(3,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(3,5-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(6-methyl-pyridine-3-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazolopyridine-2-yl)-2-pyridine carboxamide,
3-(4-ethoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(6-oxo-1,6-dihydro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide.

17. The compound which is 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

18. The compound which is 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

19. The compound which is 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

20. The compound which is 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

21. The compound which is 3-(hydroxyethyloxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

22. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

23. The compound which is 3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

24. The compound which is 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

25. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

26. The compound which is 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

27. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

28. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

29. The compound which is 3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

30. The compound which is 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

31. The compound which is 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

32. The compound which is 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

33. The compound which is 3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

34. The compound which is 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

35. Medicinal composition formed from the following (1)-(3) used in order to treat, prevent, and/or delay the onset of type II diabetes

(1) a compound represented by (I);

(2) one or more compounds selected from the group comprising (a)-(g);

(a) Other glucokinase activator.

(b). Bisguanide.

(c). PPAR agonist.

(d). Insulin.

(e). Somatostatin.

(f). α-glucosidase inhibitor.

(g). Secretion promoting agent of insulin.

(3) Pharmacologically acceptable carrier.

36. A glucokinase activator containing as an effective component, the compound in accordance with any of aforesaid 1 to 34.

37. A diabetes mellitus therapeutic and/or preventive agent, containing as an effective component, the compound in accordance with any of aforesaid 1 to 34.

38. An obesity therapeutic and/or preventive agent, containing as an effective component, the compound in accordance with any of aforesaid 1 to 34.

Ideal form for Carrying Out the Invention

Meaning of term used in this specification is described below, and further the compound in accordance with this invention is described in greater detail.

As "aryl group", hydrocarbon ring aryl group of carbon number 6-14, for example phenyl group, naphthyl group, biphenyl group, anthryl group and the like are nominated.

As "lower alkyl group", preferably alkyl group having 1-6 C straight chain or branched is meant, and for example methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group; isoamyl group, neopentyl group, isopentyl group, 1,1-dimethylpropyl group, 1-methylbutyl group, 2-methyl butyl group, 1,2-dimethylpropyl group, hexyl group, isohexyl group, 1-methyl pentyl group, 2-methyl pentyl group, 3-methyl pentyl group, 1,1-dimethylbutyl group, 1,2-dimethyl butyl group, 2,2-dimethylbutyl group, 1,3-dimethylbutyl group, 2,3-dimethyl butyl group, 3,3-dimethyl butyl group, 1-ethyl butyl group, 2-ethyl butyl group, 1,2,2-trimethylpropyl group, 1-ethyl-2-methylpropyl group and the like are nominated.

As "cycloalkyl group", 3-7C monocyclic saturated hydrocarbon group is meant, and for example cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group and the like are nominated.

As "lower alkoxy group", the group in which hydrogen atom of hydroxy group is substituted with the aforesaid lower alkyl group is meant, and for example methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, sec-butoxy group, tert butoxy group, pentyloxy group, isopentyloxy group, hexyloxy group, isohexyloxy group and the like are nominated.

As "alkyl sulphamoyl group", the group in which hydrogen atom of NH_2 of sulphamoyl group is mono substituted with said alkyl group is meant, and for example methyl sulphamoyl group, ethyl sulphamoyl group, isopropyl sulphamoyl and the like are preferred.

As "dialkyl sulphamoyl group", the group in which hydrogen atom of NH_2 of said alkyl sulphamoyl group is disubstituted with said alkyl group which is the same or different is meant, and for example dimethyl sulphamoyl group, diethyl sulphamoyl group, methylethyl sulphamoyl group and the like are

nominated.

As 'heteroaryl group", a 4-7 membered monocycle having 1-3 heteroatom selected from the group comprising oxygen atom, sulfur atom and nitrogen atom in the said heteroaryl group is meant, or bicyclic heteroaryl group in which the said monocycle heteroaryl group and pyridine ring or benzene ring are condensed is meant, and for example furyl group, thienyl group, pyrrolyl group, imidazolyl group, pyrazolyl group, thiazolyl group, thiadiazolyl group, isothiazolyl group, oxazolyl group, isoxazolyl group, pyridyl group, pyrimidinyl group, pyridazinyl group, pyrazolyl group, pyrazinyl group, quinolyl group, isoquinolyl group, quinazolinyl group, quinolidinyl group, quinoxalinyl group, cinnolinyl group, benzimidazolyl group, imidazopyridyl group, benzofuranyl group, naphthyridinyl group, 1,2-benzo isoxazolyl group, benzoxazolyl group, benzothiazolyl group, oxazolo pyridyl group, pyrido thiazolyl group, isothiazolo pyridyl group, benzothienyl group and the like are nominated.

As "halogen atom", for example fluorine atom, chlorine atom, bromine atom and iodine atom are meant.

As "lower alkyl carbamoyl group", mono substituted carbamoyl group with the aforesaid lower alkyl group is meant, and for example methylcarbamoyl group, ethyl carbamoyl group, propyl carbamoyl group, isopropyl carbamoyl group, butyl carbamoyl group, sec-butyl carbamoyl group, tert-butyl carbamoyl group and the like are nominated.

As "dilower alkyl carbamoyl group", carbamoyl group disubstituted by the same or different aforesaid lower alkyl group is meant, and as "dilower alkyl carbamoyl group", for example dimethylcarbamoyl group, diethylcarbamoyl group, ethylmethyl carbamoyl group, dipropyl carbamoyl group, methylpropyl carbamoyl group, diisopropyl carbamoyl group and the like are nominated.

As "lower alkyl amino group", amino group mono substituted by the aforesaid lower alkyl group is meant, and for example methyl amino group, ethylamino group, propylamino group, isopropyl-amino group, butyl amino group, sec-butylamino group or tert-butylamino group are nominated.

As "dilower alkyl amino group", amino group disubstituted by the same or different aforesaid lower alkyl group is meant, and for example dimethylamino group, diethylamino group, dipropylamino group, methylpropyl amino group or diisopropylamino group and the like are nominated.

As "alkanoyl group", the group in which said alkyl group and carbonyl group are bonded is meant, and

for example methyl carbonyl group, ethyl carbonyl group, propyl carbonyl group, isopropyl carbonyl group and the like are nominated.

As "alkanoyl amino group", the group in which said alkanoyl group and amino group are bonded is meant, and for example methyl carbonylamino group, ethyl carbonylamino group, isopropyl carbonylamino group and the like are nominated.

As "alkylthio group", the group in which said alkyl group and sulfur atom are bonded is meant, and for example methylthio group, ethylthio group, propylthio group, isopropylthio group and the like are nominated.

As "alkyl sulphinyl group", the group in which said alkyl group and sulphinyl group are bonded is meant, and for example methyl sulphinyl group, ethyl sulfinyl group, isopropyl sulfinyl group and the like are nominated.

As "alkylsulfonyl group", the group in which said alkyl group and sulphonyl group are bonded is meatn, and for example methylsulfonyl group, ethylsulfonyl group, propyl sulphonyl group, isopropyl sulphonyl group and the like are nominated.

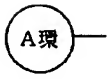
As "alkylsulfonyl amino group", the group in which hydrogen atom of amino group is mono substituted by said alkylsulfonyl group is meant, and for example methylsulphonylamino group, ethylsulfonyl amino group, propyl sulfonyl amino group or isopropyl sulfonyl amino group and the like are nominated.

As "alkoxycarbonyl group", the group in which hydrogen atom of carboxyl group is substituted with said alkyl group is meant, and for example methoxycarbonyl group, ethoxycarbonyl group, propyl oxycarbonyl group, isopropyl oxycarbonyl group and the like are nominated.

As "1-6C divalent saturated hydrocarbon group", straight or branched chain 1-6C divalent saturated hydrocarbons group is meant, and in an embodiment, for example methylene group, ethylene group, propylene group, isopropylene group, butylene group and the like are nominated.

In order to disclose further detail about the compounds represented by the aforesaid formula (I) of this invention, the various symbols used in formula (I) are explained with examples.

The A ring represented by formula (II)

ring A 

(II)

(in the formula, each symbol has the same aforesaid definitions) denotes an aryl group of a member of 5-7 membered heteroaryl group or 6-10 which may have 1 or 2 substituents selected from the group comprising lower alkyl group, lower alkoxy group, hydroxy group, hydroxyalkyl group (also hydrogen atom of hydroxy group in said hydroxyalkyl group may be substituted it by lower alkyl group) and halogen atom in said A ring.

As "5-7 membered heteroaryl group or 6-10 membered aryl group" represented by A ring, a 5 or 6 membered heteroaryl group having at least 1 of nitrogen atom in said ring is preferred.

As A ring, for example phenyl group isothiazolyl group imidazolyl group, oxazolyl group, thiadiazolyl group, thienyl group, triazolyl group, tetrazolyl group, pyridyl group, pyrimidinyl group, furyl group, thiazolyl group, isoxazolyl group or pyrazolyl group and the like are nominated, among these triazolyl group, imidazolyl group, thiazolyl group, pyridyl group are preferred, and triazolyl group is more preferable.

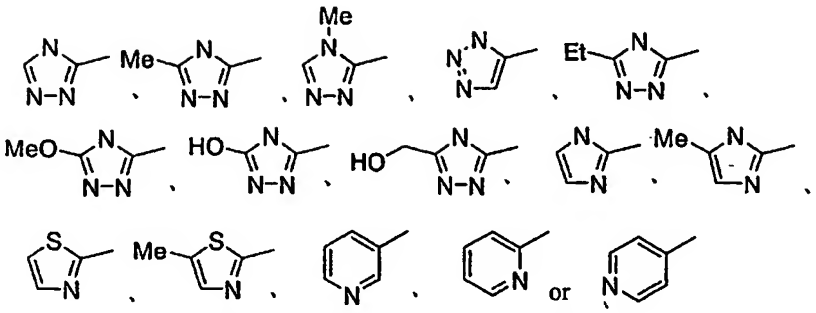
Next, the substituents on A ring are described.

A ring in the said formula (1) may have substituents on the said ring.

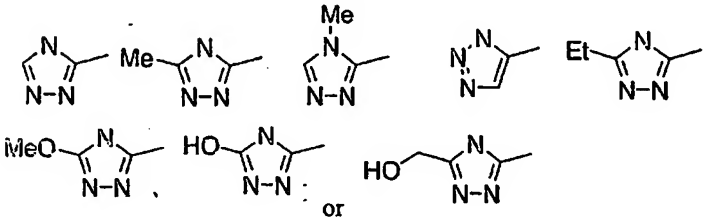
As substituents on A ring, lower alkyl alkoxy, halogen atom, hydroxy, hydroxyalkyl group (hydrogen atom of hydroxy group in hydroxyalkyl group may be substituted by alkyl group) are nominated. Among these, lower alkyl group, lower alkoxy group, hydroxy group, hydroxyalkyl group are preferred, and lower alkyl group is more preferred.

In a further embodiment, as substituent on A ring, for example methyl group, ethyl group, isopropyl group, methoxy group, ethoxy group, hydroxy group, hydroxymethyl group, hydroxyethyl group, methoxy methyl group, fluorine atom, chlorine atom and the like are nominated, methyl group of among these, ethyl group are preferred, and methyl group is more preferred.

Accordingly, as A ring as a whole, for example the groups represented by following formulae (VIII)



are preferable, and, the groups represented by following formulae (IX)

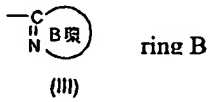


Are more preferable.

D denotes an oxygen atom or sulfur atom, but among these, it is preferred to be a sulfur atom.

Next, B ring is described.

B ring represented by the aforesaid formula (III)



(III)

is bonded with nitrogen atom of the amide group of the aforesaid formula (1), and the C=N in said ring and amide group have relative positional relationship represented by following formula (X)

(X)

and represents a monocyclic or bicyclic heteroaryl group.

The "monocyclic or bicyclic heteroaryl group" represented by B ring, has the same definition as "heteroaryl group" of aforesaid definition.

As B ring, for example, thiazolyl group, imidazolyl group, isothiazolyl group, thiadiazolyl group, triazolyl group, oxazolyl group, isoxazolyl group, pyrazinyl group, pyridyl group, pyridazinyl group, pyrazolyl group, pyrimidinyl group, pyrido thiazolyl group or benzothiazolyl group and the like are nominated, among these, thiazolyl group, thiadiazolyl group, isoxazolyl group, pyrazinyl group, pyrido thiazolyl group or pyridyl group are preferred, and thiazolyl group, thiadiazolyl group, pyrido thiazolyl group or isoxazolyl group are more preferred.

The B ring may have 1 or 2, preferably 1 substituent selected from the lower alkyl group, lower alkoxy group, halogen atom, trifluoromethyl group, hydroxy group, hydroxyalkyl group (hydrogen atom of hydroxy group in said hydroxyalkyl group may be substituted by lower alkyl group), amino alkyl group, alkanoyl group, carboxyl group, alkoxycarbonyl group and cyano group in the said ring.

As substituent on B ring, among these, lower alkyl group, lower alkoxy group, halogen atom, hydroxyalkyl group (hydrogen atom of hydroxy group in said hydroxyalkyl group may be substituted by lower alkyl group), amino alkyl group or alkanoyl group are preferred, and, lower alkyl group, hydroxyalkyl group (hydrogen atom of hydroxy group in said hydroxyalkyl group may be substituted by lower alkyl group), alkanoyl group are more preferred.

As substituent on B ring, in an embodiment, for example methyl group, ethyl group, propyl group, isopropyl group, butyl group, methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, chlorine atom, fluorine atom, bromine atom, hydroxymethyl group, hydroxyethyl group, methoxy methyl group, ethoxyethyl group, methoxyethyl group, methoxycarbonyl group, ethoxycarbonyl group, propoxy carbonyl group, aminomethyl group, aminoethyl group, aminopropyl group, methyl carbonyl group, ethyl carbonyl group, propyl carbonyl group and the like are nominated, and among these, methyl group, ethyl group, chlorine atom, fluorine atom, hydroxymethyl group, hydroxyethyl group, methoxymethyl group, methoxyethyl group, methoxycarbonyl group, ethoxycarbonyl group, aminomethyl group, aminoethyl group, methyl carbonyl group, ethyl carbonyl group, or the like are preferable, and methyl group, hydroxymethyl group, methoxymethyl group, methyl carbonyl group are more preferred.

Accordingly, as B ring as a whole, for example thiazol-2-yl group, 4-methyl-thiazol-2-yl group, 4-hydroxymethyl-thiazol-2-yl group, 4-methoxycarbonyl-thiazol-2-yl group, 4-methoxymethyl-thiazol-2-yl group, 4-aminomethyl-thiazol-2-yl group, 4-cyano-thiazol-2-yl group, 4-cyano-thiazol-2-yl group, 4-fluoro-thiazol-2-yl group, imidazol-2-yl group, 4-methyl-imidazol-2-yl group, 4-methoxycarbonyl-imidazol-2-yl group, iso thiazol-3-yl group, 4-hydroxymethyl-iso thiazol-3-yl group, [1,3,4] thiadiazol-2-yl group, 5-methyl carbonyl-[1,3,4] thiadiazol-2-yl group, [1,2,4] thiadiazol-5-yl group, 3-methyl-[1,2,4] thiadiazol-5-yl group, [1,2,41 triazol-2-yl group, 5-hydroxymethyl-[1,2,4] triazol-3-yl group, pyrazin-2-yl group, pyridin-2-yl group, 4-methyl-pyridin-2-yl group, 4-methoxymethyl-imidazol-2-yl group, 4-methyl carbonyl-imidazol-2-yl group, 5-hydroxymethyl-imidazol-2-yl group, 5-methyl-[1,3,4] thiadiazol-2-yl group, 5-fluoro-[1,3,4] thiadiazol-2-yl group, 5-methyl-[1,2,4] triazol-2-yl group, 5-methyl carbonyl-[1,2,4] triazol-3-yl group, isoxazol-3-yl group, 4-methoxymethyl-isoxazol-2-yl group-5-methyl-isoxazol-3-yl group, 5-hydroxymethyl-isoxazol-3-yl group, 5-methoxymethyl-isoxazol-3-yl group, 5-methyl carbonyl-isoxazol-3-yl group, 5-chloro-isoxazol-3-yl group, 5-aminomethyl-isoxazol-3-yl group, 4 methyl-1H-pyrazol-3-yl group, 1-methyl-pyrazol-3-yl group, 6-methyl-pyridazin-3-yl group, thiazol-4-yl group, 2-methyl-thiazol-4-yl group, isoxazol-3-yl group, pyrido thiazole group and the like are preferred.

X1 denotes a nitrogen atom, sulfur atom or oxygen atom, or a divalent saturated hydrocarbons group of carbon number 1-6.

Wherein, as "divalent saturated hydrocarbons group of 1-6C", a 1-6 C alkylene group of the said definition is meant, and for example methylene group, propylene group, isopropylene group, butylene group are nominated. Moreover, when the carbon number of said divalent saturated hydrocarbon group is 2-6, any one of carbon atom in said divalent saturated hydrocarbons group may be replaced by nitrogen atom, sulfur atom or oxygen atom.

In a further embodiment, as X1, for example, nitrogen atom, oxygen atom, sulfur atom, $-CH_2-$, $-N-CH_2-$, $-S-CH_2-$, $-O-CH_2-$, $-CH_2-N-$, $-CH_2-S-$ or $-CH_2-CO-$ and the like are nominated, among these, preferably X1 is nitrogen atom, sulfur atom, oxygen atom, $-N-CH_2-$ or CH_2-, and it is more preferred to be sulfur atom.

R2 and R3 may be the same or different, and denote a hydrogen atom, lower alkyl group, alkoxy group halogen atom.

The "lower alkyl group" represented by R2 and R3, may be the same or different, and methyl group or

ethyl group is preferred, and more preferably, R2 and R3 are both methyl groups.

The "lower alkoxy group" represented by R2 and R3, may be the same or different and preferably denote ethoxy group or methoxy group, and it is more preferred that R2 and R3 are both methoxy groups.

As "halogen atom" represented by R2 and R3, fluorine atom, chlorine atom or bromine atom is preferred, and fluorine atom or chlorine atom is more preferred.

As R2 and R3, preferably R2 and R3 are both hydrogen atoms.

R1 means 6-10 membered aryl group, 5-10 membered heteroaryl group, 3-7C cycloalkyl group or lower alkyl group. The "6-10 membered aryl group" represented by R1 either denotes hydrocarbon ring aryl group of carbon number of 6-10 members, or a 9-10 membered bicyclic group formed by condensation of 5 or 6 membered aliphatic hetero ring having 1 or 2 heteroatoms selected from nitrogen atom, sulfur atom and oxygen atom in the ring (said aliphatic heterocycle may be substituted by oxy group) and benzene ring.

As said 6-10 membered hydrocarbon ring aryl group, for example, phenyl group, naphthyl group, biphenyl group and the like are nominated, and among these, phenyl group is preferred.

As said 9-10 membered bicyclic aryl group, in a further embodiment, for example ethylenedioxy phenyl group, methylenedioxyphenyl group, tetrahydroquinolinyl group, tetrahydroiso quinolinyl group, dihydroindolyl group, 2,3-dihydrobenzofuranyl group, 1,3-dihydroisobenzofuranyl group, oxy indolyl group, isoindolyl group and the like are nominated, and among these ethylenedioxy phenyl group or tetrahydroiso quinolinyl group is preferred.

The "5-10 membered heteroaryl group" represented by R1 denotes a 5-7 membered monocyclic heteroaryl group or a 9-10 membered bicyclic heteroaryl group having 1-3 heteroatoms selected from oxygen atom, nitrogen atom and sulfur atom in said ring.

As said 5-7 membered monocyclic heteroaryl group, in a further embodiment, for example isoxazolyl group, isothiazolyl group, imidazolyl group, oxazolyl group, thiazolyl group, thiadiazolyl group, thienyl group, triazolyl group, tetrazolyl group, pyridyl group, pyrazinyl group, pyrimidinyl group, pyridazinyl group, pyrazolyl group, pyrrolyl group, pyranyl group, furyl group, furazanyl group,

imidazolidinyl group and the like are nominated.

As said 9-10 membered bicyclic heteroaryl group, in a further embodiment, for example isoquinolyl group, isoindolyl group, indolyl group, quinolyl group, pyrido thiazolyl group, benzimidazolyl group, benzoxazolyl group, benzothiazolyl group, benzotriazolyl group, benzofuranyl group, imidazo pyridinyl group, tri azo pyridinyl group and the like are nominated.

Among said 5-10 membered heteroaryl group, a 5-7 membered monocyclic heteroaryl group is preferred, and as a further embodiment pyridyl group, imidazolyl group, thiazolyl group, thienyl group are preferred.

As "cycloalkyl group of carbon number 3-7" represented by R1, the same groups as the said definition are nominated, and among these, cyclopentyl group or cyclohexyl group is preferred.

As "lower alkyl group" represented by R1, the same groups as the said definition are nominated, and among these, propyl group and butyl group are preferred.

As R1, a 6-10 membered aryl group, 5-10 membered heteroaryl group and 3-7 membered cycloalkyl group are preferred, and a 6-10 membered aryl group and 5-10 membered heteroaryl group are more preferred.

In an embodiment, for example phenyl group, naphthyl group, biphenyl group, isoxazolyl group, isothiazolyl group, imidazolyl group, oxazolyl group, thiazolyl group, titanium azolyl group, thienyl group, triazolyl group, tetrazolyl group, pyridyl group, pyrazinyl group, pyrimidinyl group, pyridazinyl group, pyrazolyl group, pyrrolyl group, pyranyl group, furyl group, furazanyl group, imidazolidinyl group, isoquinolyl group, isoindolyl group, indolyl group, ethylenedioxy phenyl group, methylenedioxyphenyl group, quinolyl group, pyrido thiazolyl group, dihydroindolyl group, tetrahydroquinolinyl group, tetrahydroiso quinolinyl group, benzimidazolyl group, benzoxazolyl group, benzothiazolyl group, benzotriazolyl group, benzofuranyl group, cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, methyl group, ethyl group, propyl group, isopropyl group, butyl group, pentyl group and the like nominated, among these, phenyl group naphthyl group, pyridyl group, imidazolyl group, thiazolyl group, thienyl group, cyclopentyl group, cyclohexyl group and the like are preferred, and phenyl group, pyridyl group, imidazolyl group, thiazolyl group, thienyl group are even more preferred and phenyl group or pyridyl group is preferred furthermore.

Thereafter the substituents of R1 are described.

As the substituent which R1 has, hydrogen atom, amino group, hydroxy group, hydroxyalkyl group (hydrogen atom of said hydroxy group may be substituted by lower alkyl group), lower alkyl group (hydrogen atom in said lower alkyl group may be substituted by hydroxy group, alkoxy group, amino group, alkylamino group, dialkylamino group, halogen atom, carbamoyl group, mono or dialkylcarbamoyl group, carboxyl group, alkoxycarbonyl group or alkanoyl group), lower alkoxy group (the hydrogen group in methyl group or methylene group constituting the said lower alkoxy group may be substituted by hydroxy group, alkoxy group, amino group, alkylamino group, dialkylamino group, halogen atom, carbamoyl group, mono or di-lower alkyl carbamoyl group, carboxyl group, alkoxycarbonyl group or alkanoyl group), carbamoyl group, alkyl carbamoyl group, dialkyl carbamoyl group, carbamoyloxy group, carbamoyl amino group, cyano group, sulphamoyl group, trifluoromethyl group, halogen atom, formyl group, C2-6C alkanoyl group, N-C2-6C alkanoyl amino group, C1-6C alkylthio group, N-C1-6C alkyl sulphamoyl group, N,N-di-C1-6C alkyl sulphamoyl group, C1-6C alkyl sulphinyl group, C1-6C alkylsulfonyl group, N-C1-6C alkylsulfonyl amino group, C1-6C alkoxycarbonyl group, C1-6C alkylamino group or N,N-C1-C6-di-alkylamino group are nominated.

R1 may have hydroxyalkyl group as substituent. As said hydroxyalkyl group, for example, hydroxymethyl group, hydroxyethyl group, hydroxypropyl group, hydroxy isopropyl group, hydroxybutyl group, hydroxy pentyl group and the like are preferred, and hydroxymethyl group, hydroxyethyl group, hydroxypropyl group, hydroxy isopropyl group are more preferred.

Moreover, the hydrogen atom of said hydroxy group may be substituted by lower alkyl group of 1-6C, and, as the aforesaid substituted hydroxyalkyl group, for example methoxy methyl group, 1-methoxyethyl group, ethoxymethyl group, methoxyethyl group, propyl oxymethyl group and the like are nominated, among these, methoxy methyl group and methoxyethyl group are preferred, and methoxy methyl group is more preferred.

R1 may have lower alkyl group as substituent. As said lower alkyl group, the same groups as lower alkyl group of the said definition are nominated, among these, methyl group, ethyl group, propyl group, butyl group, isopropyl group or the like are preferred, and methyl group, ethyl groups and the like are more preferred.

When R1 has a lower alkyl group as substituent, the hydrogen atom in said lower alkyl group may be substituted by hydroxy group, lower alkoxy group, amino group, mono alkyl amino group or dialkylamino group. As said lower alkyl group, for example hydroxymethyl group, hydroxyethyl group, methoxy methyl group, ethoxymethyl group, methoxyethyl group, aminomethyl group, amino ethyl group, aminopropyl group, methylaminomethyl group, ethylamino methyl group, dimethylaminomethyl group, ethyl-methylaminomethyl group, aminomethyl group, 2-amino-ethyl group, 1-amino-ethyl group, 3-amino-propyl group, 2-amino-1-methyl-methyl group, 2-amino-propyl group, 4-amino-butyl group, 2-amino-1-methyl-propyl group, 2-amino-butyl group, 5-amino-pentyl group, 3-amino-1,2-dimethyl-propyl group, 6-amino-hexyl group and the like are nominated, among these, aminomethyl group, 2-amino-ethyl group, 1-amino-ethyl group, 3-amino-propyl group, 3-amino-1-methyl-ethyl group, 2-amino-propyl group are preferred, and 2-amino-ethyl group or 3-aminopropyl group is more preferred.

R1 may have lower alkoxy group as substituent (1 of hydrogen atom in said lower alkoxy group may be substituted by hydroxy group or amino group).

As said alkoxy group, the same groups as in alkoxy group of the said definition are nominated, among these, methoxy group, ethoxy group, propoxy group, isopropoxy group and the like are preferred, and methoxy group or ethoxy group is more preferred. When the hydrogen atom in said alkoxy group is substituted by hydroxy group, for example 2-hydroxy-ethoxy group, 3-hydroxy-propoxy group, 4-hydroxy-butoxy group, 2-hydroxy-1-methyl-ethoxy group, 2-hydroxy-propoxy group, 3-hydroxy-2-methyl-propoxy group, 3-hydroxy-butoxy group and the like are nominated, and among these, for example 2-hydroxy-ethoxy group, 3-hydroxy-propoxy group, 2-hydroxy-1-methyl-ethoxy group and the like are preferred, and 2-hydroxyethoxy group is more preferred.

When hydrogen atom in said alkoxy group is substituted by amino group, said amino group may be further substituted by 1 or 2 lower alkyl groups. When said amino group is substituted by two lower alkyl groups, said lower alkyl groups may be the same or different, and alkylamino alkoxy group or dialkylamino alkoxy group is preferred, and dialkylamino ethoxy group is more preferred.

In a further embodiment, for example amino ethoxy group, methylamino ethoxy group, dimethylaminoethoxy group, dimethylamino propoxy group and the like are nominated, among these, methylamino ethoxy group or dimethylaminoethoxy group are preferred, and dimethylaminoethoxy group is more preferred.

R1 may have a lower alkyl carbamoyl group as substituent. As said lower alkyl carbamoyl group, the same groups as in lower alkyl carbamoyl group of the said definition are nominated, a lower alkyl carbamoyl group of 1-5 C is preferred, and 1-3 C lower alkyl carbamoyl group is more preferred. In a further embodiment, as said lower alkyl carbamoyl group, for example methylcarbamoyl group, ethyl carbamoyl group, propyl carbamoyl group and the like are preferred, and methylcarbamoyl group is more preferred.

R1 may have dilower alkyl carbamoyl group as substituent. As said dilower alkyl carbamoyl group, the same groups as in dilower alkyl carbamoyl group of the said definition are nominated, for example dimethylcarbamoyl group, diethylcarbamoyl group, ethylmethylcarbamoyl group are nominated, and dimethylcarbamoyl group is more preferred.

R1 may have halogen atom as substituent. As said halogen atom, the same atoms as in halogen atom of the said definition are nominated, for example fluorine atom, chlorine atom, bromine atom and the like are nominated, and among these, fluorine atom or chlorine atom is more preferred.

R1 may have C2-C6 alkanoyl group as substituent. As said C2-6C alkanoyl group, the same alkanoyl groups as in C2-C6 alkanoyl group of the said definition are nominated, as a further embodiment for example methyl carbonyl group, ethyl carbonyl group, propyl carbonyl group or isopropyl carbonyl group are preferred, and methyl carbonyl group or ethyl carbonyl group is more preferred.

R1 may have N-C2-C6-alkanoyl amino group as substituent. In a further embodiment, as said N-C2-C6-alkanoyl group, for example ethyl carbonylamino group, propyl carbonylamino group, isopropyl carbonylamino group and the like are preferred, and methyl carbonylamino group, ethyl carbonylamino group are more preferred.

R1 may have C1-6C alkylthio group as substituent. As said alkylthio group, the same groups same as in alkylthio group of the said definition are nominated. In a further embodiment, as said alkylthio group, for example methylthio group, ethylthio group, propylthio group, isopropylthio group and the like are preferred, and methylthio group and ethylthio group are more preferred.

R1 may have alkyl sulphamoyl group as substituent. As said alkyl sulphamoyl group, the same groups as in the aforesaid definition are nominated. As said alkyl sulphamoyl group, for example methyl sulphamoyl group, ethyl sulphamoyl group, propyl sulphamoyl group and the like are preferred, and methyl sulphamoyl group and ethyl sulphamoyl group are more preferred.

R1 may have dialkyl sulphamoyl group as substituent. As said dialkyl sulphamoyl group, the same groups as in the aforesaid definition are nominated. In a further embodiment, as said dialkyl sulphamoyl group, for example dimethyl sulphamoyl group, diethyl sulphamoyl group and the like are preferred, and dimethyl sulphamoyl group is more preferred.

R1 may have alkyl sulfinyl group as substituent. As said alkyl sulfinyl group, the same groups as in the aforesaid definition are nominated. In a further embodiment, as said alkyl sulphinyl group, for example methylsulfinyl group, ethyl sulphinyl group, propyl sulphinyl group, isopropyl sulfinyl group and the like are preferred, and methyl sulphinyl group and ethyl sulphinyl group are more preferred.

R1 may have alkylsulfonyl group as substituent. As said alkylsulfonyl group, the same groups as in the aforesaid definition are nominated. In a further embodiment, as said alkylsulfonyl group, for example methylsulfonyl group, ethylsulfonyl group, propyl sulphonyl group, isopropyl sulphonyl group and the like are preferred, and methylsulfonyl group and ethylsulfonyl group are more preferred.

R1 may have alkylsulfonyl amino group as substituent. As said alkylsulfonyl amino group, the same groups as in the aforesaid definition are nominated. In a further embodiment, as said alkylsulfonyl amino group, for example methylsulphonylamino group, ethylsulfonyl amino group, propyl sulfonyl amino group, isopropyl sulfonyl amino group and the like are preferred, and methylsulphonylamino group and ethylsulfonyl amino group are more preferred.

R1 may have alkoxycarbonyl group as substituent. As far as said alkoxycarbonyl group, the same groups as in the aforesaid definition are nominated. Further in an embodiment, as said alkoxycarbonyl group, for example methoxycarbonyl group, ethoxycarbonyl group, isopropoxy carbonyl group, propoxy carbonyl group and the like are preferred, and methoxycarbonyl group and ethoxycarbonyl group are more preferred.

R1 may have alkylamino group as substituent. As said alkylamino group, the same groups as in the aforesaid definition are nominated. In a further embodiment, as said alkylamino group, for example methylamino group, ethylamino group and the like are preferred, and methylamino group is more preferred.

R1 may have N,N-di-C1-6C alkylamino group as substituent. As N,N-di-C1-6C alkylamino group, for example dimethylamino group, diethylamino group, ethyl-methyl-amino group are preferred, and

dimethylamino group is more preferred.

R1 may have cyclic amino group of 5 or 6 members as substituent. As said cyclic amino group of 5 or 6 members, the same groups as in aforesaid definition of "cyclic amino group" are nominated. As "substituent of R1", for example pyrrolidinyl group, piperazinyl group or morpholinyl group and the like are preferred, and piperidinyl group or morpholinyl group is more preferred.

As substituent of R1, among these, hydrogen atom, hydroxyalkyl group, lower alkyl group, lower alkoxy group, carbamoyl group, alkylcarbamoyl group, cyano group, trifluoromethyl group, halogen atom, C2-6C alkanoyl group, N-C2-6C alkanoyl amino group, C1-6C alkylsulfonyl group, C1-6C alkylamino group or amino alkyl group are preferred, and lower alkyl group, lower alkoxy group, alkylcarbamoyl group, halogen atom, C1-6C alkylsulfonyl group or amino alkyl group are more preferred.

Accordingly, as a further embodiment as -X1-R1, for example, phenyl sulphanyl group, 4-hydroxyethyl-phenyl sulphanyl group, 3-hydroxymethyl-phenyl sulphanyl group, 2-hydroxymethyl-phenyl sulphanyl group, 4-methyl-phenyl sulphanyl group, 3-methyl-phenyl sulphanyl group, 2-methyl-phenyl sulphanyl group, 4-isopropyl-phenyl sulphanyl group, 4-methoxy-phenyl sulphanyl group, 4-methoxymethyl-phenyl sulphanyl group, 3-methoxy-phenyl sulphanyl group, 2-ethoxy-phenyl sulphanyl group, 4-ethoxy-phenyl sulphanyl group, 4-hydroxymethyl-phenyl sulphanyl group, 4-hydroxyethyl oxy-phenyl sulphanyl group, 4-carbamoyl-phenyl sulphanyl group, 4-methylcarbamoyl-phenyl sulphanyl group, 4-dimethylcarbamoyl-phenyl sulphanyl group, 4-isopropyl carbamoyl-phenyl sulphanyl group, 4-cyano-phenyl sulphanyl group, 4-trifluoromethyl-phenyl sulphanyl group, 4-fluoro-phenyl sulphanyl group, 3-chloro-phenyl sulphanyl group, 2-fluoro-phenyl sulphanyl group, 4-methyl carbonyl-phenyl sulphanyl group, 4-ethyl carbonyl-phenyl sulphanyl group, 3-methyl carbonyl-phenyl sulphanyl group, 3-ethyl carbonyl-phenyl sulphanyl group, 4-methyl carbonylamino-phenyl sulphanyl group, 4-ethyl carbonyl-phenyl sulphanyl group, 4-isopropyl carbonyl-phenyl sulphanyl group, 4-methylsulfonyl-phenyl sulphanyl group, 3-ethylsulfonyl-phenyl sulphanyl group, 4-methylsulfonyl-phenyl sulphanyl group, 4-isopropyl sulfonyl-phenyl sulphanyl group, 4-methylamino-phenyl sulphanyl group, 3-ethylamino-phenyl sulphanyl group, 2-methylamino-phenyl sulphanyl group, 4-aminomethyl-phenyl sulphanyl group, 3-aminomethyl-phenyl sulphanyl group, 4-amino ethyl-phenyl sulphanyl group, 4-dimethylaminoethyl oxy-phenyl sulphanyl group, thiazol-2-yl-sulphanyl group, 4-hydroxymethyl-thiazol-2-yl group, 5-hydroxymethyl-thiazol-2-yl-sulphanyl group, 4-hydroxyethyl-thiazol-2-yl-sulphanyl group, 4-methyl-thiazol-2-yl-sulphanyl group, 5-methyl-thiazol-2-yl-sulphanyl group, 4-ethyl-thiazol-2-yl-sulphanyl group, 4-methoxy-thiazol-2-yl-sulphanyl group, 4-ethoxy-

thiazol-2-yl-sulphanyl group, 4-carbamoyl-thiazole-2 yl-sulphanyl group, 5-carbamoyl-thiazol-2-yl-sulphanyl group, 4-methylcarbamoyl-thiazol-2-yl-sulphanyl group, 4-ethyl carbamoyl-thiazol-2-yl-sulphanyl group, 4-isopropyl-thiazol-2-yl-sulphanyl group, 4-cyano-thiazol-2-yl-sulphanyl group, 4-chloro-thiazol-2-yl-sulphanyl group, 4-fluoro-thiazol-2-yl-sulphanyl group, 4-methyl carbonyl-thiazol-2-yl-sulphanyl group, 4-ethyl carbonyl-thiazol-2-yl-sulphanyl group, 4-ethyl carbonylamino-thiazol-2-yl-sulphanyl group, 4-methyl carbonylamino-thiazol-2-yl-sulphanyl group, 4-methylsulfonyl-thiazol-2-yl-sulphanyl group, 4-ethylsulfonyl-thiazol-2-yl-sulphanyl group, 3-methylsulfonyl-thiazol-2-yl-sulphanyl group, 4-isopropyl-sulfonyl-thiazol-2-yl-sulphanyl group, 4-methylamino-thiazol-2-yl-sulphanyl group, 3-methylamino-thiazol-2-yl-sulphanyl group, 4-ethylamino-thiazol-2-yl-sulphanyl group, 4-aminomethyl-thiazol-2-yl-sulphanyl group, 4-amino ethyl-thiazol-2-yl-sulphanyl group, pyridine-2-yl-sulphanyl group, pyridine-3-yl-sulphanyl group, pyridine-4-yl-sulphanyl group, 6-hydroxymethyl-pyridine-3-yl-sulphanyl group, 4-hydroxymethyl-pyridine-5-yl-sulphanyl group, 4-hydroxymethyl-pyridine-6-yl-sulphanyl group, 3-hydroxymethyl-pyridine-6-yl-sulphanyl group, 4-methyl-pyridine-5-yl-sulphanyl group, 4-methyl-pyridine-6-yl-sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group, 6-methoxy-pyridine-3-yl-sulphanyl group, 6-ethoxy-pyridin-3-yl sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group, 2-carbamoyl-pyridine-4-yl-sulphanyl group, 6-carbamoyl-pyridine-3-yl-sulphanyl group, 6-methylcarbamoyl-pyridine-3-yl-sulphanyl group, 2-methylcarbamoyl-pyridine-4-yl-sulphanyl group, 2-cyano-pyridine-4-yl-sulphanyl group, 6-cyano-pyridine-3-yl-sulphanyl group, 2-trifluoromethyl-pyridine-4-yl-sulphanyl group, 6-trifluoromethyl-pyridine-3-yl-sulphanyl group, 2-chloro-pyridine-4-yl-sulphanyl group, 6-chloro-pyridine-3-yl-sulphanyl group, 2-fluoro-pyridine-4-yl-sulphanyl group, 6-fluoro-pyridine-3-yl-sulphanyl group, 2-methyl carbonyl-pyridine-4-yl-sulphanyl group, 6-methyl carbonyl-pyridine-3-yl-sulphanyl group, 2-ethyl carbonyl-pyridine-4-yl-sulphanyl group, 6-ethyl carbonyl-pyridine-3-yl-sulphanyl group, 2-methylsulfonyl-pyridine-4-yl-sulphanyl group, 6-methylsulfonyl-pyridine-3-yl-sulphanyl group, 2-ethylsulfonyl-pyridine-4-yl-sulphanyl group, 6-isopropyl sulfonyl-pyridine-3-yl-sulphanyl group, 2-methyl carbonylamino-pyridine-4-yl-sulphanyl group, 6-methyl carbonylamino-pyridine-3-yl-sulphanyl group, 2-methylamino-pyridine-4 yl-sulphanyl group, 6-methylamino-pyridine-3-yl-sulphanyl group, 2-ethylamino-pyridine-4-yl-sulphanyl group, 6-ethylamino-pyridine-3-yl-sulphanyl group, 2-aminomethyl-pyridine-4-yl-sulphanyl group, 6-aminomethyl-pyridine-3-yl-sulphanyl group, 4-hydroxyethyl-phenylamino group, 3-hydroxymethyl-phenylamino group, 2-hydroxymethyl-phenylamino group, 4-methyl-phenylamino group, 3-methyl-phenylamino group, 2-methyl-phenylamino group, 4-ethyl-phenylamino group, 4-isopropyl-phenylamino group, 4-methoxy-phenylamino group, 3-methoxy-phenylamino group, 2-ethoxy-phenylamino group, 4-ethoxy-phenylamino group, 4-hydroxymethyl-phenylamino group, 4-carbamoyl-phenylamino group, 4-methylcarbamoyl-phenylamino group, 4-isopropyl carbamoyl-phenylamino group, 4-cyano-

phenylamino group, 4-trifluoromethyl-phenylamino group, 4-fluoro-phenylamino group, 3-chloro-phenylamino group, 2-fluoro-phenylamino group, 4-methyl carbonyl-phenylamino group, 4-ethyl carbonyl-phenylamino group, 3-methyl carbonyl-phenylamino group, 3-ethyl carbonyl-phenylamino group, 4-methyl carbonylamino-phenylamino group, 4-ethyl carbonylamino-phenylamino group, 4-isopropyl carbonylamino-phenylamino group, 4-methylsulfonyl-phenylamino group, 3-ethylsulfonyl-phenylamino group, 4-isopropyl sulfonyl-phenylamino group, 4-methylamino-phenylamino group, 3-ethylamino-phenylamino group, 4-aminomethyl-phenylamino group, 3-aminomethyl-phenylamino group, 4-amino ethyl-phenylamino group, 3-amino ethyl-phenylamino group, 4-methyl-thiazole-ylamino group, 5-methyl-thiazol-2-ylamino group, 4-ethyl-thiazol-2-ylamino group, 5-ethyl-thiazol-2-ylamino group, 4-ethoxy-thiazol-2-ylamino group, 5-methoxy-thiazol-2-ylamino group, 4-carbamoyl-thiazol-2-ylamino group, 5-carbamoyl-thiazol-2-ylamino group, 4-methylcarbamoyl-thiazol-2-ylamino group, 4-ethyl carbamoyl-thiazol-2-ylamino group, 4-methyl-thiazol-2-ylamino group, 4-ethyl-thiazol-2-ylamino group, 4-cyano-thiazol-2-ylamino group, 4-chloro-thiazol-2-ylamino group, 4-fluoro-thiazol-2-ylamino group, 4-methylcarbamoyl-thiazol-2-ylamino group, 4-ethyl carbamoyl-thiazol-2-ylamino group, 4-isopropyl-thiazol-2-ylamino group, 4-cyano-thiazol-2-ylamino group, 4-chloro-thiazol-2-ylamino group, 4-fluoro-thiazol-2-ylamino group, 4-methyl carbonyl-thiazol-2-ylamino group, 4-ethyl carbonyl-thiazol-2-ylamino group, 4-ethyl carbonylamino-thiazol-2-ylamino group, 4-methyl carbonylamino-thiazol-2-ylamino group, 4-methylsulfonyl-thiazol-2-ylamino group, 4-ethylsulfonyl-thiazol-2-ylamino group, 3-methylsulfonyl-thiazol-2-ylamino group, 4-isopropyl-sulfonyl-thiazol-2-ylamino group, 4-methylamino-thiazol-2-ylamino group, 3-methylamino-thiazol-2-ylamino group, 4-ethylamino-thiazol-2-ylamino group, 4-aminomethyl-thiazol-2-ylamino group, 4-amino ethyl-thiazol-2-ylamino group, 3-aminomethyl-thiazol-2-ylamino group, pyridine-4-ylamino group, 6-hydroxymethyl-pyridine-3-ylamino group, 3-hydroxymethyl-pyridine-4-ylamino group, 4-hydroxymethyl-pyridine-2-ylamino group, 5-hydroxymethyl-pyridine-2-ylamino group, 3-methyl-pyridine-4-yl-sulphanyl group, 4-methyl-pyridine-2-ylamino group, 6-methyl-pyridine-3-ylamino group, 6-methoxy-pyridine-3-ylamino group, 6-methyl-pyridine-3-ylamino group, 2-carbamoyl-pyridine-4-ylamino group, 6-carbamoyl-pyridine-3-ylamino group, 6-methylcarbamoyl-pyridine-3-ylamino group, 2-methylcarbamoyl-pyridine-4-ylamino group, 2-cyano-pyridine-4-ylamino group, 6-cyano-pyridine-3-ylamino group, 2-trifluoromethyl-4-ylamino group, 6-trifluoromethyl-pyridine-3-ylamino group, 2-chloro-pyridine-4-ylamino group, 6-chloro-pyridine-3-ylamino group, 2-fluoro-pyridine-4-ylamino group, 6-fluoro-pyridine-3-ylamino group, 2-methyl carbonyl-pyridine-4-ylamino group, 6-methyl carbonyl-pyridine-3-ylamino group, 2-ethyl carbonyl-pyridine-4-ylamino group, 6-ethyl carbonyl-pyridine-3-ylamino group, 2-methylsulfonyl-pyridine-4-ylamino group, 6-methylsulfonyl-pyridine-3-ylamino group, 2-ethylsulfonyl-pyridine-4-ylamino group, 6-isopropyl sulfonyl-pyridine-3-ylamino group, 2-methyl carbonylamino-pyridine-4-ylamino group, 6-methyl

carbonylamino-pyridine-3-ylamino group, 2-methylamino-pyridine-4 ylamino group, 6-methylamino-pyridine-3-ylamino group, 2-ethylamino-pyridine-4-ylamino group, 6-ethylamino-pyridine-3-ylamino group, 2-aminomethyl-pyridine-4-ylamino group, 6-aminomethyl-pyridine-3-ylamino group, 4-hydroxymethyl-phenoxy group, 4-hydroxyethyl-phenoxy group, 3-hydroxymethyl-phenoxy group, 3-hydroxyethyl-phenoxy group, 4-methyl-phenoxy group, 3-ethyl-phenoxy group, 4-methoxy-phenoxy group, 3-methoxy-phenoxy group, 4-ethoxy-phenoxy group, 4-carbamoyl-phenoxy group, 3-carbamoyl-phenoxy group, 4-methylcarbamoyl-phenoxy group, 3-isopropyl carbamoyl-phenoxy group, 4-cyano-phenoxy group, 3-cyano-phenoxy group, 4-trifluoromethyl-phenoxy group, 3-trifluoromethyl-phenoxy group, 4-chloro-phenoxy group, 3-chloro-phenoxy group, 4-fluoro-phenoxy group, 3-fluoro-phenoxy group, 4-methyl carbonyl-phenoxy group, 3-methyl carbonyl-phenoxy group, 4-ethyl carbonyl-phenoxy group, 4-methyl carbonylamino-phenoxy group, 3-methyl carbonylamino-phenoxy group, 4-methylsulfonyl-phenoxy group, 3-methylsulfonyl-phenoxy group, 4-ethylsulfonyl-phenoxy group, 3-ethylsulfonyl-phenoxy group, 4-methylamino-phenoxy group, 3-methylamino-phenoxy group, 4-ethylamino-phenoxy group, 3-ethylamino-phenoxy group, 4-aminomethyl-phenoxy group, 3-aminomethyl-phenoxy group, 4-amino ethyl-phenoxy group, 3-amino ethyl-phenoxy group, 4-hydroxyethyl-phenylmethyl amino group, 3-hydroxymethyl-phenylmethyl amino group, 2-hydroxymethyl-phenylmethyl amino group, 4-methyl-phenylmethyl amino group, 3-methyl-phenylmethyl amino group, 2-methyl-phenylmethyl amino group, 4-ethyl-phenylmethyl amino group, 4-isopropyl-phenylmethyl amino group, 4-methoxy-phenylmethyl amino group, 3-methoxy-phenylmethyl amino group, 2-ethoxy-phenylmethyl amino group, 4-ethoxy-phenylmethyl amino group, 4-hydroxymethyl-phenylmethyl amino group, 4-carbamoyl-phenyl methylamino group, 4-methylcarbamoyl-phenylmethyl amino group, 4-isopropyl carbamoyl-phenylmethyl amino group, 4-cyano-phenylmethyl amino group, 4-trifluoromethyl-phenylmethyl amino group, 4-fluoro-phenylmethyl amino group, 3-chloro-phenylmethyl amino group, 2-chloro-phenylamino methyl group, 2-fluoro-phenylmethyl amino group, 4-methyl carbonyl-phenylmethyl amino group, 4-ethyl carbonyl-phenylmethyl amino group, 3-methyl carbonyl-phenylmethyl amino group, 3-ethyl carbonyl-phenylmethyl amino group, 4-methyl carbonylamino-phenylmethyl amino group, 4-ethyl carbonylamino-phenylmethyl amino group, 4-isopropyl carbonylamino-phenylmethyl amino group, 4-methylsulfonyl-phenylmethyl amino group, 3-ethylsulfonyl-phenylmethyl amino group, 4-isopropyl sulfonyl-phenylmethyl amino group, 4-methylamino-phenylmethyl amino group, 3-ethylamino-phenylmethyl amino group, 4-aminomethyl-phenylmethyl amino group, 3-aminomethyl-phenylmethyl amino group, 4-amino ethyl-phenylmethyl amino group, 3-amino ethyl-phenylmethyl amino group, 4-methyl-thiazole-ylmethyl amino group, 5-methyl-thiazol-2-ylmethyl amino group, 4-ethyl-thiazol-2-ylmethyl amino group, 5-ethyl-thiazol-2-yl methylamino group, 4-ethoxy-thiazol-2-ylmethyl amino group, 5-methoxy-thiazol-2-yl methylamino group, 4-carbamoyl-thiazol-2-ylmethyl amino group, 5-

carbamoyl-thiazol-2-ylmethyl amino group, 4-methylcarbamoyl-thiazol-2-ylmethyl amino group, 4-ethyl carbamoyl-thiazol-2-yl methylamino group, 4-methyl-thiazole-2 yl methylamino group, 4-ethyl-thiazol-2-ylmethyl amino group, 4-cyano-thiazol-2-yl methylamino group, 4-chloro-thiazol-2-yl methylamino group, 4-fluoro-thiazol-2-yl methylamino group, 4-methylcarbamoyl-thiazol-2-ylmethyl amino group, 4-ethyl carbamoyl-thiazole-2 yl methylamino group, 4-isopropyl-thiazol-2-yl methylamino group, 4-cyano-thiazol-2-yl methylamino group, 4-chloro-thiazol-2-yl methylamino group, 4-fluoro-thiazol-2-yl methylamino group, 4-methyl carbonyl-thiazol-2-ylmethyl amino group, 4-ethyl carbonyl-thiazol-2-yl methylamino group, 4-ethyl carbonylamino-thiazol-2-yl methylamino group, 4-methyl carbonylamino-thiazol-2-yl methylamino group, 4-methylsulfonyl-thiazol-2-yl methylamino group, 4-ethylsulfonyl-thiazol-2-ylmethyl amino group, 3-methylsulfonyl-thiazol-2-yl methylamino group, 4-isopropyl-sulfonyl-thiazol-2-yl methylamino group, 4-methylamino-thiazole-2-yl methylamino group, 3-methylamino-thiazol-2-ylmethyl amino group, 4-ethylamino-thiazol-2-yl methylamino group, 4-aminomethyl-thiazol-2-yl methylamino group, 4-amino ethyl-thiazol-2-ylmethyl amino group, 3-aminomethyl-thiazol-2-yl methylamino group, pyridine-4-ylmethyl amino group, 6-hydroxymethyl-pyridin-3-yl methylamino group, 3-hydroxymethyl-pyridin-4-yl methylamino group, 4-hydroxymethyl-pyridine-2-ylmethyl amino group, 5-hydroxymethyl-pyridin-2-yl methylamino group, 3-methyl-pyridine-4-yl-sulphanyl group, 4-methyl-pyridin-2-yl methylamino group, 6-methyl-pyridin-3-yl methylamino group, 6-methoxy-pyridino-3-ylmethyl amino group, 6-methyl-pyridin-3-yl methylamino group, 2-carbamoyl-pyridine-4-ylmethyl amino group, 6-carbamoyl-pyridine-3-ylmethyl amino group, 6-methylcarbamoyl-pyridine-3-ylmethyl amino group, 2-methylcarbamoyl-pyridin-4-yl methylamino group, 2-cyano-pyridine-4-ylmethyl amino group, 6-cyano-pyridin-3-yl methylamino group, 2-trifluoromethyl-4-yl methylamino group, 6-trifluoromethyl-pyridin-3-yl methylamino group, 2-chloro-pyridin-4-yl methylamino group, 6-chloro-pyridin-3-yl methylamino group, 2-fluoro-pyridine-4-ylmethyl amino group, 6-fluoro-pyridin-3-yl methylamino group, 2-methyl carbonyl-pyridin-4-yl methylamino group, 6-methyl carbonyl-pyridin-3-yl methylamino group, 2-ethyl carbonyl-pyridin-4-yl methylamino group, 6-ethyl carbonyl-pyridin-3-yl methylamino group, 2-methylsulfonyl-pyridine-4-ylmethyl amino group, 6-methylsulfonyl-pyridin-3-yl methylamino group, 2-ethylsulfonyl-pyridin-4-yl methylamino group, 6-isopropyl sulfonyl-pyridin-3-yl methylamino group, 2-methyl carbonylamino-pyridin-4-yl methylamino group, 6-methyl carbonylamino-pyridin-3-yl methylamino group, 2-methylamino-pyridin-4-yl methylamino group, 6-methylamino-pyridine-3-ylamino group, 2-ethylamino-pyridine-4-ylamino group, 6-ethylamino-pyridine-3-ylamino group, 2-aminomethyl-pyridine-4-ylamino group, 6-aminomethyl-pyridin-3-yl methylamino group, 3-hydroxymethyl-phenylmethyl group, 2-hydroxymethyl-phenylmethyl group, 4-methyl-phenylmethyl group, 3-methyl-phenylmethyl group, 2-methyl-phenylmethyl group, 4-methyl-phenylmethyl group, 4-isopropyl-phenylmethyl group, 4-methoxy-phenylmethyl group, 3-methoxy-phenylmethyl group, 2-

ethoxy-phenylmethyl group, 4-ethoxy-phenylmethyl group, 4-hydroxymethyl-phenylmethyl group, 4-carbamoyl-phenylmethyl group, 4-methylcarbamoyl-phenylmethyl group, 4-isopropyl carbamoyl-phenylmethyl group, 4-cyano-phenylmethyl group, 4-trifluoromethyl-phenylmethyl group, 4-fluoro-phenylmethyl group, 3-chloro-phenylmethyl group, 2-fluoro-phenylmethyl group, 4-methyl carbonyl-phenylmethyl group, 4-ethyl carbonyl-phenylmethyl group, 3-methyl carbonyl-phenylmethyl group, 3-ethyl carbonyl-phenylmethyl group, 4-methyl carbonylamino-phenyl methyl group, 4-ethyl carbonyl-phenylmethyl group, 4-isopropyl carbonyl-phenylmethyl group, 4-methylsulfonyl-phenylmethyl group, 3-ethylsulfonyl-phenylmethyl group, 4-methylsulfonyl-phenylmethyl group, 4-isopropyl sulfonyl-phenylmethyl group, 4-methylamino-phenylmethyl group, 3-ethylamino-phenylmethyl group, 2-methylamino-phenylmethyl group, 4-aminomethyl-phenylmethyl group, 3-aminomethyl-phenylmethyl group, 4-amino ethyl-phenylmethyl group, thiazol-2-ylmethyl group, 4-hydroxymethyl-thiazol-2-yl group, 5-hydroxymethyl-thiazol-2-yl methyl group, 4-hydroxyethyl-thiazol-2-ylmethyl group, 4-methyl-thiazol-2-yl methyl group, 5-methyl-thiazol-2-yl methyl group, 4-ethyl-thiazol-2-yl methyl group, 4-methoxy-thiazol-2-ylmethyl group, 4-ethoxy-thiazol-2-yl methyl group, 4-carbamoyl-thiazole-2 ylmethyl group, 5-carbamoyl-thiazol-2-yl methyl group, 4-methylcarbamoyl-thiazol-2-ylmethyl group, 4-ethyl carbamoyl-thiazole-2-ylmethyl group, 4-isopropyl-thiazol-2-yl methyl group, 4-cyano-thiazol-2-yl methyl group, 4-chloro-thiazole-2-ylmethyl group, 4-fluoro-thiazol-2-ylmethyl group, 4-methyl carbonyl-thiazol-2-yl methyl group, 4-ethyl carbonyl-thiazol-2-ylmethyl group, 4-ethyl carbonylamino-thiazol-2-ylmethyl group, 4-methyl carbonylamino-thiazol-2-yl methyl group, 4-methylsulfonyl-thiazol-2-yl methyl group, 4-ethylsulfonyl-thiazol-2-yl methyl group, 3-methylsulfonyl-thiazol-2-yl methyl group, 4-isopropyl-sulfonyl-thiazol-2-ylmethyl group, 4-methylamino-thiazol-2-ylmethyl group, 3-methylamino-thiazol-2-yl methyl group, 4-ethylamino-thiazol-2-yl methyl group, 4-aminomethyl-thiazol-2-yl methyl group, 4-amino ethyl-thiazol-2-yl methyl group, pyridin-4-yl methyl group, 6-hydroxymethyl-pyridin-3-yl methyl group, 3-hydroxymethyl-pyridine-4-ylmethyl group, 4-hydroxymethyl-pyridin-2-yl methyl group, 6-hydroxymethyl-pyridin-3-yl methyl group, 3-methyl-pyridine-4-yl-sulphanyl group, 4-methyl-pyridin-2-yl methyl group, 6-methyl-pyridin-3-yl methyl group, 6-methoxy-pyridine-3-yl methyl group, 6-methyl-pyridin-3-yl methyl group, 2-carbamoyl-pyridine-4-yl methyl group, 6-carbamoyl-pyridin-3-yl methyl group, 6-methylcarbamoyl-pyridin-3-yl methyl group, 2-methylcarbamoyl-pyridine-4-yl methyl group, 2-cyano-pyridin-4-yl methyl group, 6-cyano-pyridine-3-yl methyl group, 2-trifluoromethyl-4-yl methyl group, 6-trifluoromethyl-pyridin-3-yl methyl group, 2-chloro-pyridin-4-yl methyl group, 6-chloro-pyridin-3-yl methyl group, 2-fluoro-pyridin-4-yl methyl group, 6-fluoro-pyridin-3-yl methyl group, 2-methyl carbonyl-pyridin-4-yl methyl group, 6-methyl carbonyl-pyridin-3-yl methyl group, 2-ethyl carbonyl-pyridin-4-yl methyl group, 6-ethyl carbonyl-pyridin-3-yl methyl group, 2-methylsulfonyl-pyridin-4-yl methyl group, 6-methylsulfonyl-pyridin-3-yl methyl group, 2-

ethylsulfonyl-pyridin-4-yl methyl group, 6-isopropyl sulfonyl-pyridine-3-yl methyl group, 2-methyl carbonylamino-pyridin-4-yl methyl group, 6-methyl carbonylamino-pyridin-3-yl methyl group, 2-methylamino-pyridine-4-ylmethyl group, 6-methylamino-pyridine-3-yl amino group, 2-ethylamino-pyridine-4-ylamino group, 2-ethylamino-pyridine-5-ylamino group, 2-aminomethyl-pyridine-4-ylamino group, 6-aminomethyl-pyridin-3-yl methyl group and the like are nominated.

Among these,

phenyl sulphanyl group, 4-hydroxyethyl-phenyl sulphanyl group, 4-methyl-phenyl sulphanyl group, 3-methyl-phenyl sulphanyl group, 4-methoxy-phenyl sulphanyl group, 3-methoxy-phenyl sulphanyl group, 4-ethoxy-phenyl sulphanyl group, 4-hydroxymethyl-phenyl sulphanyl group, hydroxyethyl oxy-phenyl sulphanyl group, 4-carbamoyl-phenyl sulphanyl group, 4-methylcarbamoyl-phenyl sulphanyl group, 4-dimethylcarbamoyl-phenyl sulphanyl group, 4-cyano-phenyl sulphanyl group, 4-trifluoromethyl-phenyl sulphanyl group, 4-fluoro-phenyl sulphanyl group, 3-chloro-phenyl sulphanyl group, 2-fluoro-phenyl sulphanyl group, 4-methyl carbonyl-phenyl sulphanyl group, 4-ethyl carbonyl-phenyl sulphanyl group, 4-methyl carbonylamino-phenyl sulphanyl group, 4-methylsulfonyl-phenyl sulphanyl group, 4-methylamino-phenyl sulphanyl group, 4-aminomethyl-phenyl sulphanyl group, 4-amino ethyl-phenyl sulphanyl group, 4-dimethylaminoethyl oxy-phenyl sulphanyl group, thiazol-2-yl-sulphanyl group, 4-methyl-thiazol-2-yl-sulphanyl group, 5-methyl-thiazol-2-yl-sulphanyl group, pyridine-4-yl-sulphanyl group, pyridine-3-yl-sulphanyl group, pyridine-2-yl-sulphanyl group, 6-hydroxymethyl-pyridine-3-yl-sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group, 6-methoxy-pyridine-3-yl-sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group, 6-carbamoyl-pyridine-3-yl-sulphanyl group, 6-methylcarbamoyl-pyridine-3-yl-sulphanyl group, 2-cyano-pyridine-4-yl-sulphanyl group, 6-cyano-pyridine-3-yl-sulphanyl group, 6-trifluoromethyl-pyridine-3-yl-sulphanyl group, 2-chloro-pyridine-4-yl-sulphanyl group, 6-chloro-pyridine-3-yl-sulphanyl group, 2-fluoro-pyridine-4-yl-sulphanyl group, 6-fluoro-pyridine-3-yl-sulphanyl group, 6-methyl carbonyl-pyridine-3-yl-sulphanyl group, 6-ethyl carbonyl-pyridine-3-yl-sulphanyl group, 6-methylsulfonyl-pyridine-3-yl-sulphanyl group, 6-methyl carbonylamino-pyridine-3-yl-sulphanyl group, 6-methylamino-pyridine-3-yl-sulphanyl group, 6-ethylamino-pyridine-3-yl-sulphanyl group, 6-aminomethyl-pyridine-3-yl-sulphanyl group, 4-methyl-phenylamino group, 4-methoxy-phenylamino group, 4-fluoro-phenylamino group, 4-methyl-thiazol-2-ylamino group, 5-methyl-thiazol-2-ylamino group, pyridine-4-ylamino group, 2-methyl-pyridine-5-ylamino group, 4-methyl-phenoxy group, 4-methoxy-phenoxy group, 4-fluoro-phenoxy group, 4-methyl-phenylamino methyl group, 3-methyl-phenylamino methyl group, 2-methyl-phenylamino methyl group, 4-fluoro-phenylaminomethyl group, 2-chloro-phenylmethyl amino group, 2-fluoro-phenylamino methyl group, 4-methyl-thiazol-2-ylamino methyl group, 5-methyl-thiazol-2-ylamino methyl group, pyridine-4-ylamino methyl group, 6-methyl-pyridine-3-ylaminomethyl group, 2-methyl-pyridine-5-ylamino methyl group, 4-methyl-phenylmethyl group, 4-methoxy-phenylmethyl

group, 4-fluoro-phenylmethyl group are preferred,

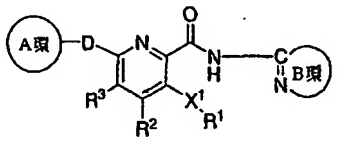
more preferably,

phenyl sulphanyl group, 4-hydroxyethyl-phenyl sulphanyl group, 4-methyl-phenyl sulphanyl group, 3-methyl-phenyl sulphanyl group, 4-methoxy-phenyl sulphanyl group, 3-methoxy-phenyl sulphanyl group, 4-ethoxy-phenyl sulphanyl group, 4-hydroxymethyl-phenyl sulphanyl group, hydroxyethyl oxy-phenyl sulphanyl group, 4-carbamoyl-phenyl sulphanyl group, 4-methylcarbamoyl-phenyl sulphanyl group, 4-dimethylcarbamoyl-phenyl sulphanyl group, 4-cyano-phenyl sulphanyl group, 4-trifluoromethyl-phenyl sulphanyl group, 4-fluoro-phenyl sulphanyl group, 3-chloro-phenyl sulphanyl group, 2-fluoro-phenyl sulphanyl group, 4-methyl carbonyl-phenyl sulphanyl group, 4-methylsulfonyl-phenyl sulphanyl group, 4-dimethylaminoethyl oxy-phenyl sulphanyl group, pyridine-4-yl-sulphanyl group, pyridine-3-yl-sulphanyl group, 6-methoxy-pyridine-3-yl-sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group, 6-trifluoromethyl-pyridine-3-yl-sulphanyl group,

and still more preferably,

phenyl sulphanyl group, 4-hydroxyethyl-phenyl sulphanyl group, 4-methyl-phenyl sulphanyl group, 4-methoxy-phenyl sulphanyl group, 4-ethoxy-phenyl sulphanyl group, 4-methylcarbamoyl-phenyl sulphanyl group, 4-dimethylcarbamoyl-phenyl sulphanyl group, 4-cyano-phenyl sulphanyl group, 4-trifluoromethyl-phenyl sulphanyl group, 4-fluoro-phenyl sulphanyl group, 2-fluoro-phenyl sulphanyl group, 4-methyl carbonyl-phenyl sulphanyl group, 4-methylsulfonyl-phenyl sulphanyl group, 4-dimethylaminoethyl oxy-phenyl sulphanyl group, pyridine-4-yl-sulphanyl group, pyridine-3-yl-sulphanyl group, 6-methoxy-pyridine-3-yl-sulphanyl group, 6-methyl-pyridine-3-yl-sulphanyl group.

In accordance with the above, as further embodiments of the compound represented by formula (I) in accordance with this invention

ring A  ring B

(I)

(each symbol has the same aforesaid definitions)

for example, compound which is

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-imidazol-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(thiazol-2-yl-sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(2-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-phenyl sulphanyl-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyloxy)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenylmethyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(3-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(2,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-cyano-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(pyridine-4-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-acetyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(thiophene-2-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-

pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridinecarboxamide,

3-(4-methyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-chloro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(3H-[1,2,3] triazol-4-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methylsulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-hydroxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methoxymethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-trifluoromethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-dimethylaminomethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methyl sulfamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide,

3-(4-hydroxy-cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridazine-3-yl)-2-pyridinecarboxamide,

3-(pyrazine-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-[4-(1-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-phenoxy-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(2-chloro-phenylmethyl-amino)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3,6-bis-(pyridine-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3,6-bis-(4-fluoro-phenyl sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3,6-bis-(thiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3,6-bis-(5-methyl-[1,3,4] thiadiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,3,4] thiadiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl carbonyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrimidine-4-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridine-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-ethoxycarbonyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methoxy-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-phenyloxy methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazole-2 yl)-2-pyridinecarboxamide,

3-phenyl sulphanyl methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-phenylmethyl-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenylmethyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminomethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-4-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(4-hydroxyethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methoxy carbonyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(pyrimidin-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-hydroxymethyl-pyridine-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-[4-(1-methyl-pyrrolidine-3-yloxy)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-diethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-pyrrolidino ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-dimethylaminoethyl oxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(pyrazol-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-carbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(5-bromo-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-

thiadiazol-5-yl)-2-pyridinecarboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-still-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazole-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,5] thiadiazol-3-yl)-2-pyridinecarboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methoxy-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-cyclopropyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazole-3-yl sulphanyl-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(2-fluoro-pyridin-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(2-methoxy-pyrimidin-5-yl sulphanyl)-6-(2H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-diethylcarbamoyl methyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-cyclopropyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(pyrazol-4-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylamino sulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(5-fluoro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazine-3-yl)-2-pyridinecarboxamide,

3-(4-carboxy-phenyl sulphanyl)-6-(5-methyl-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide,

3-(imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(2-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [4,5-b] pyridine-2-yl)-2-pyridinecarboxamide,

3-(5-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4,4-difluoromethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(6-hydroxyethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(2-methyl-imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-hydroxymethyl-[1,2,4]-

thiadiazol-5-yl)-2-pyridinecarboxamide,

3-[4-(2-hydroxyethyl)-phenyl sulphanyl]-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(1-methyl-1H-indazol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(3-methyl-[1,2,4]-triazolo-[4,3-a]-pyridin-7-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-[4-(1H-imidazole-1 yl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-[4,5-dimethyl thiazol-2-yl]-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4,5-dimethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-(1-methoxyethyl)-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl) 2-pyridinecarboxamide,

3-(pyridine-4-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl) 2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-chloro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(3H-[1,2,3] triazol-4-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,3,4] thiadiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methylsulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-hydroxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazole-3 yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-N,N-dimethylamino-ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-2-yl)-2-pyridinecarboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide or the like is more preferably,

and moreover, the compound which is

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl) 2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-N,N-dimethylamino-ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-2-yl)-2-pyridinecarboxamide,
3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazole-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,
3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,
3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide,
3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,41 triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide,
3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide,
3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide or the like is more preferred.

Moreover, pyridine-2-carboxamide derivative in accordance with this invention is possible to present as pharmacologically acceptable salt. As aforesaid salt, acid addition salt or base addition salt is nominated.

As for the compound in accordance with this invention, there are case that stereoisomers such as optical isomers, diastereoisomers, geometric isomers or the like or tautomer are present due to the forms of substituents thereof. Needless to say that these isomers are all included in the compounds in accordance with this invention. Needless to say that arbitrary mixture of isomers thereof is also included by the compound in accordance with this invention.

Because the compound of this invention have glucokinase activation action, it is useful as therapeutic drug and/or prevnetive drug of diabetes cases, moreover, as therapeutic drug and/or prevnetive drug of diabetic complications.

Wherein, diabetic complications are diseases that develop as a result of diabetes mellitus, and as said diabetic complications, for example diabetic nephropathy, diabetic retinopathy, diabetic neurosis, diabetic arteriosclerosis and the like are nominated.

The compound in accordance with this invention can be applited to either type of diabetes mellitus of insulin-dependent diabetes mellitus (IDDM) and non-insulin dependent diabetes mellitus (NIDDM).

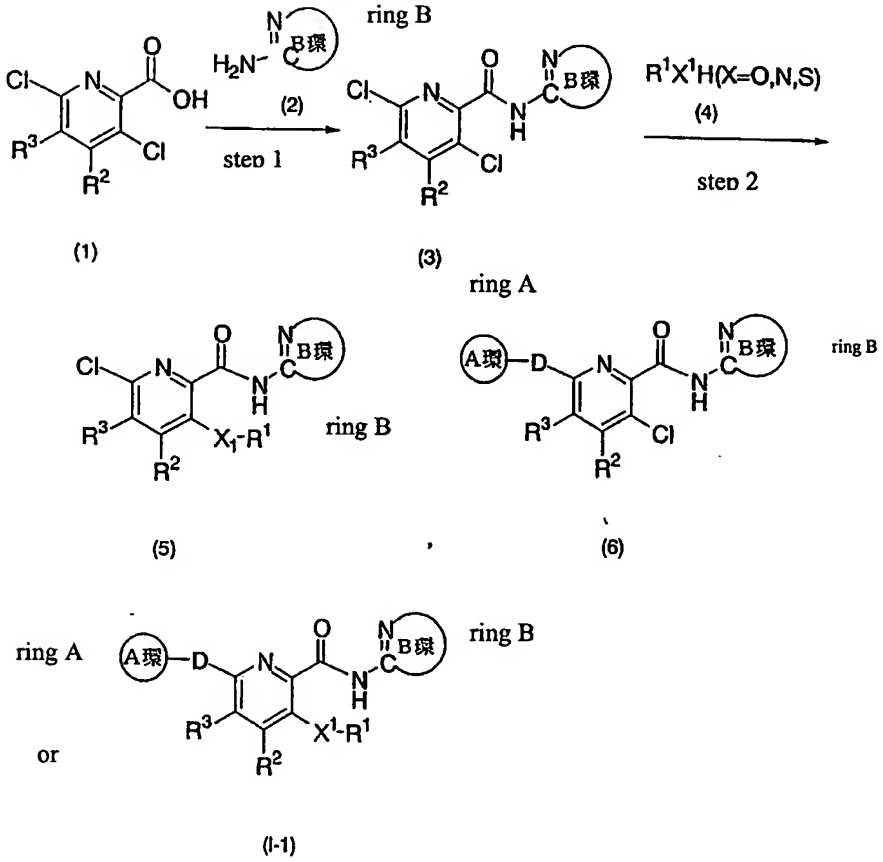
Moreover, the insulin-dependent diabetes mellitus (IDDM) is considered mainly as adult onset wherein the onset is cuased by addition of insulin resistance due to obesity to the predisposition of hereditary low insulin secretion and insulin resistance inskeletal muscle. Moreover, as for the aforesaid insulin-dependent diabetes mellitus, classifications of type I and type II have been proposed by predisposition thereof.

The compound in accordance with this invention is considered to be useful in type II diabetes mellitus in which the satisfactory lowering of blood glucose level was not thought to be possible with prior art diabetes mellitus drug, in addition to type I insulin-dependent diabetes mellitus.

Moreover, in type II diabetes mellitus, the level of postprandial hyperglycemia is maintained over a long period compared to healthy person. However, the compound in accordance with this invention is useful for this type II diabetes mellitus.

Below, a process for the production of the compound in accordance with this invention is described.

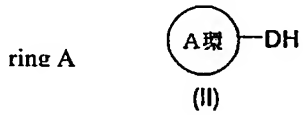
The compound in accordance with this invention (I) can be readily produced by using well known reaction means or by according to itself well-known method. Moreover, as for the compound in accordance with this invention (I) can be produced not only by a synthesis method in ordinary liquid phase, but also by processed using solid phase for example combinatorial synthesis method, parallel synthesis method or the like which have been developed remarkably in reccent years. The compound in accordance with this invention can be produced preferably using for example following process.



(wherein, each symbol has the same aforesaid definitions).

(Step 1).

This step comprises a process wherein, dichloropyridine carboxylic acid derivative or its reactive derivative and amino compound (2) are reacted, and compound (3) is produced.



Amide formation reaction may be carried out by the method according to the literature (for example, basis and practice of peptide synthesis, Nobuo Izumiya, Comprehensive Organic Synthesis, Vol. 6, Pergamon Press, 1991), a method based on this, or a combination of these with conventional method, namely, using a condensing agent known to a person skilled in the art, or an ester activation method

which can be used by a person skilled in the, mixed anhydride method, acid chloride method, carbodiimide method and so on.

As such amide forming reagent, for example thionyl chloride, oxalyl chloride, N,N-dicyclohexylcarbodiimide, 1-methyl-2-bromo pyridinium iodide, N,N'-carbonyldiimidazole, diphenyl phosphoryl chloride, diphenyl phosphoryl acid, N,N'-disuccinimidyl carbonate, N,N'-disuccinimidyl oxalate, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, ethylchloroformate, isobutyl chloroformate or benzotriazol-1-yl-oxy-tris (dimethylamino) phosphonium hexafluoro phosphite and the like are nominated, and wherein for example thionyl chloride, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, N,N-dicyclohexylcarbodiimide or benzotriazol-1-yl-oxy-triazol-1-yloxytris(dimethylamino) phosphonium hexafluoro phosphite and the like are ideal. Moreover, in amide forming reaction, base, condensation assistant may be used with the aforesaid amide forming reagent.

As the base which is used, for example tertiary aliphatic amine such as trimethylamine, triethyl amine, N,N-diisopropyl ethylamine, N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N,N-dimethylaniline, 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU), 1,5-azabicyclo [4.3.0] non-5-ene (DBN) or the like; for example aromatic amine and the like such as pyridine, 4-dimethylaminopyridine, picoline, lutidine, quinoline or isoquinoline and the like are nominated, wherein for example tertiary aliphatic amine and the like are preferred, and in particular for example triethylamine or N,N-diisopropyl ethylamine and the like is ideal.

As the condensation assistant which is used, for example N-hydroxybenzotriazole hydrate, N-hydroxy succinimide, N-hydroxy-5-norbornene-2,3-dicarboximide or 3-hydroxy-3,4-dihydro-4-oxo-1,2,3-benzotriazole and the like are nominated, wherein for example N-hydroxybenzotriazole and the like is ideal.

The quantity of compound (2) which is used differs depending on the compounds and kinds of solvent, and other reaction conditions used, but it is usually 0.1-10 equivalents, preferably 0.5-3 equivalents with respect to 1 equivalent of carboxylic acid (1) or a reactive derivative thereof.

The quantity of amide forming reagent used differs depending on the compounds and kinds of solvent, and other reaction conditions used, but it is usually 1-10 equivalents, preferably 1-3 equivalents with respect to carboxylic acid compound (1) or reactive derivative thereof.

The quantity of condensation assistant used differs depending on the compounds and kinds of solvent, and other reaction conditions, but it is usually 1-10 equivalents, preferably 1-3 equivalents with respect to 1 equivalent of carboxylic acid compound (1) or a reactive derivative thereof.

The quantity of base used differs depending on the compounds and kinds of solvent, and other reaction conditions, but it is usually 1-10 equivalents, preferably 1-5 equivalents.

As the reaction solvent used in this step, for example inert solvent is nominated, which does not hinder the reaction, in particular is not restricted, however, in an embodiment, for example methylene chloride, chloroform, 1,2-dichloroethane, N,N-dimethylformamide, ethyl acetate, methyl acetate, acetonitrile, benzene, xylene, toluene, 1,4,-dioxane, tetrahydrofuran, dimethoxyethane or a mixed solvent thereof is nominated, but for example methylene chloride, chloroform, 1,2-dichloroethane, acetonitrile or N,N-dimethylformamide and the like are preferred from the point of maintaining a suitable reaction temperature.

Usually reaction temperature is -78°C to boiling point of solvent temperature, preferably 0-30°C in this step.

The reaction time is usually 0.5-96 hours, preferably 3-24 hours in this step.

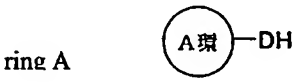
One or a combination of bases, amide forming reagents, condensation assistants may be used in this step.

When substituent on B ring of compound (3) produced in this step has a protecting group, the aforesaid protecting group can be removed in accordance with requirements. The aforesaid removal of protecting groups can be carried out by combining process in accordance with literature method (Protective Groups In 0rganlc Synthesis, T.W.Green Author-the second edition, John Wiley & Sons Co, 1991, or the like), or these combined with conventional method.

Compound (3) obtained in this way can be isolated and purified by using well known separation and refinement means, for example concentration, vacuum concentration, crystallization, solvent extraction, reprecipitation, chromatography and the like, or can be subjected to next step without being isolated and purified

(Step 2).

This step comprises a process wherein, in the presence of base, (5) or (6) or (I-1) is produced by reaction of the compound (3) obtained in the said step 1 with a compound (4) represented by R1X1H (X1 denotes an oxygen atom, nitrogen atom or sulfur atom and R1 is same as in the aforesaid definition) or a compound represented by formula (II).



(II)

(wherein, each symbol has the same aforesaid definitions)

As compound (4) used in this reaction, phenol derivative, thiol derivative or amine derivative is used. Wherein, the phenol derivative includes not only the case where a hydroxy group was bonded to aryl group, but also when hydroxy group was bonded to 5-7 membered heteroaryl group.

In this step, when compound (4) was used, it is possible to produce compound (5).

The formula (II-1) is a phenol derivative or thiol derivative where DH (D represents oxygen atom or sulfur atom) was bonded to A ring of the aforesaid compound (II).
(Wherein, phenol derivative has the same as the aforesaid definition).

In the step, when the compound (II) was used in this step, it is possible to produce compound (6) or (I-1).

The compound (I-1) are the compounds included by compound (1) in accordance with this invention.

In this step, the quantity of compound (4) or (II) used is usually 0.2-10 equivalents, preferably 1-3 equivalents with respect to 1 equivalent of compound (3).

As the base used in this step, tertiary aliphatic amine such as for example trimethylamine, triethylamine, N,N-diisopropyl ethylamine, N-methylmorpholine, N-methylpyrrolidine, N-methylpiperidine, N,N-dimethylaniline, 1,8-diazabicyclo [5.4.0] undec-7-en (DBU) 1,5-azabicyclo [4.3.0] non-5-ene (DBN) or the like; aromatic amine such as for example pyridine, 4-dimethylaminopyridine, picoline, lutidine, aromatic amine such as for example quinoline or isoquinoline and the like; alkali metal such as for example metallic potassium, metallic sodium, metallic lithium and the like; alkali metal hydride such as for example sodium hydride, potassium

hydride and the like; alkyl alkali metal such as for example butyllithium and the like; alkali metal alkoxide such as for example potassium-tert butylate, sodium ethylate or sodium methylate and the like; alkali metal hydroxide such as for example potassium hydroxide, sodium hydroxide and the like; alkali metal carbonate and the like such as for example potassium carbonate, sodium carbonate, cesium carbonate and the like are nominated, wherein for example tertiary aliphatic amine, alkali metal hydride, alkali metal carbonate or alkali metal alkoxide is preferred, and in particular, for example triethylamine, N,N-diisopropyl ethylamine, sodium hydride or potassium carbonate, alkali metal alkoxide such as for example potassium-tert butylate, sodium ethylate or sodium methylate and the like are ideal.

In this step, the quantity of base used differs depending on the compound and kind of solvent, it is usually 0.2-10 equivalents, preferably 1-5 equivalents with respect to 1 equivalent of compound (3).

As the reaction solvent which is used, it is not restricted in particular provided it does not hinder the reaction. However, for example inert organic solvent is preferred. Furthermore in an embodiment, for example methylene chloride, chloroform, 1,2-dichloroethane, trichloroethane, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, acetone, ethanol, isopropanol, tert butanol, tert amyl alcohol, ethyl acetate ester, methyl acetate, acetonitrile, benzene, xylene, toluene, 1,4,-dioxane, tetrahydrofuran, dimethoxyethane or a mixed solvent thereof is nominated, N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone, acetonitrile, isopropanol, tert amyl alcohol and the like are preferred, and N,N-dimethylformamide, acetonitrile, isopropanol and the like is more preferred.

The reaction time is usually 0.2-100, preferably 1-40 hours.

Usually the reaction temperature is -20°C to boiling point of solvent temperature, preferably 0°C to boiling point of solvent temperature.

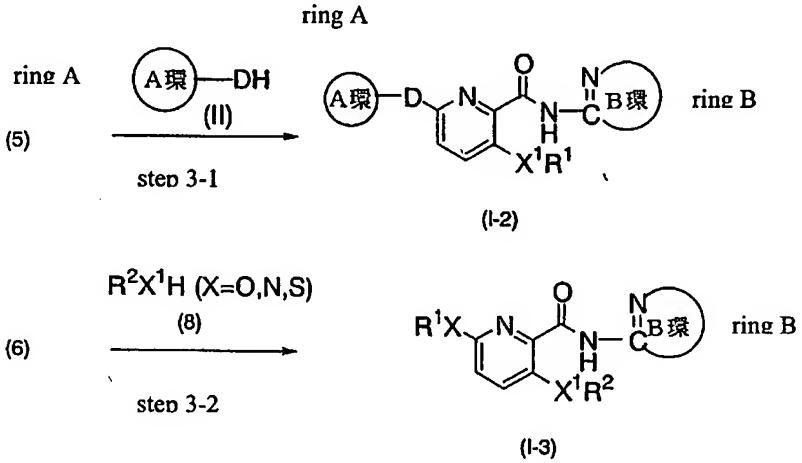
Moreover, in this step, catalyst and additive can be added to the process mentioned in accordance with literature (Organic letters 2002, Vol. 4, 20, pp. 3517-3520), or the method based on this, or a combination of of these with conventional methods.

As the catalyst used in this step, any which accelerates the reaction can be used, but for example copper chloride, copper bromide, copper iodide, copper oxide, copper acetate and the like are nominated, among these copper iodide is more preferred.

Moreover, as the additive used in this step, any which advances the reaction can be, but for example ethylene glycol, dimethoxyethane and the like are nominated, ethylene glycol of among these is more preferred.

Compound (5) or (6) obtained in this way can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, reprecipitation, solvent extraction, crystallization, chromatography and the like, or can be subjected to next step without being isolated and purified

Moreover, the compound in accordance with this invention (I-1) can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, reprecipitation, solvent extraction, crystallization, chromatography and the like.



(in the formula, each symbol has the same aforesaid definitions).

(Step 3-1).

This step comprises a process wherein, by reacting the compound (5) obtained in the said step 2 with a phenol derivative or thiol derivative having A ring represented the said formula (II)

(in the formula, each symbol has the same aforesaid definitions) in the presence of base, the compound (I-2) in accordance with this invention is produced.

This step can be carried out by a process using the equivalent quantity of the compound, the reaction solvent, the reaction time, reaction conditions such as for example reaction temperature or the like same as in the said step 2.

The compound obtained in this way (I-1) can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like, or it can be subjected to next step without being isolated and purified.

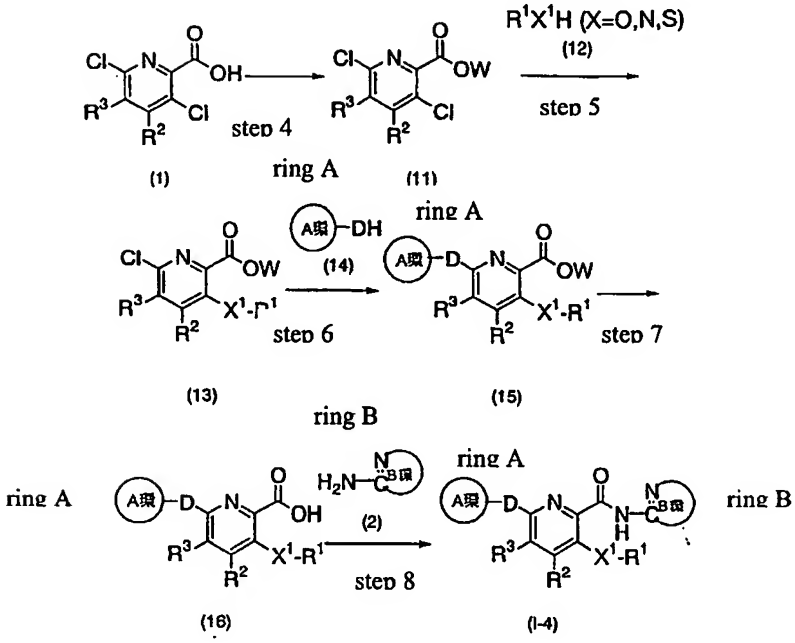
(Step 3-2).

This step comprises a process wherein, by reacting compound (6) obtained in the said step 2 with the compound (4) represented by R1XIH (in the formula, each symbol has the same aforesaid definitions), the compound (I-3) is produced.

The compound used in this step, equivalent quantity of base, the reaction solvent reaction time, reaction conditions such as for example reaction temperature or the like are the same as the aforesaid step 2, and can be reacted in this step using the same process as in the said step 2.

The compound obtained in this way (I-3) is isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, crystallization, solvent extraction, reprecipitation, chromatography, or it can be subjected to next step without isolation and purification.

Moreover, the compound in accordance with this invention (I-4) can be produced by following process.



(W represents a carboxy protecting group, and other symbols mean the same as in the aforesaid definition).

(Step 4).

This step is a process to produce compound (11) by introducing protecting group to the carboxyl group which dichloropyridine-2-carboxylic acid derivative (1) has. Compound (11) can be produced by well known method or method in accordance with it. The protecting group W of the carboxylic acid group in (11) is not particularly limited, but can be any group which acts as a protecting group in step 5 and step 6, and can be deprotected readily in step 7. A lower alkyl group having branched or straight chain such as for example methyl group, ethyl group, tert-butyl group and the like, lower haloalkyl such as for example 2-iodoethyl group, 2,2,2-trichloroethyl group and the like, lower alkenyl group such as for example allyl group, 2-propenyl group, 2-methyl-2-propenyl group and the like, aralkyl group such as for example benzyl group, PMB group or the like are nominated.

About introduction and removal process of protecting group W of such carboxyl group, it can be carried out by process in accordance with literature (for example Protective Groups in Organic Synthesis, TW green author, 2nd edition, John Wiley and Sons, 1991 etc.), method based on this or a combination of these and conventional method.

Compound (11) obtained in this way can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, reprecipitation, crystallization, chromatography, or it can be subjected to next step without being isolated and purified

(Step 5).

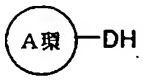
This step comprises a process wherein compound (13) is produced by reacting compound (11) represented by R1X1H (in the formula, each symbol has the same aforesaid definitions) with compound (12) obtained in the said step 4.

In this step, reaction conditions such as for example the compounds used in this step, equivalent quantity of base, reaction solvent reaction temperature, the reaction time or the like can be the same as in the said step 2.

Compound (13) obtained in this way can be isolated and purified by using well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography., or can be subjected to next step without being isolated and purified

(Step 6).

This step comprises a process wherein compound (15) is produced by reacting compound (13) obtained in the said step 5 with phenol derivative or thiol derivative represented by following formula (II)

ring A 

(II)

(in the formula, each symbol has the same aforesaid definitions). Wherein, phenol derivative has the same definition as the aforesaid definition.

This step can be carried out by process same as in the said step 2 using an equivalent quantity of the compound, the quantity of base, the reaction time, reaction temperature, the reaction solvent. Compound (15) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for

example concentration, vacuum concentration, reprecipitation, solvent extraction, crystallization, chromatography and the like.

(Step 7).

This step comprises a process wherein compound (16) is produced by removing the protecting group W of the carboxyl group from the compound (15) obtained in the said step 6.

In this step, the removal reaction of protecting group W of carboxyl group can be carried out by a process in accordance with literature (Protective Groups in Organic Synthesis, T.W. Green, 2nd Edition.John Wiley & Sons Co, 1991, or the like), a method in accordance with this, or a combination of these with conventional method.

Compound (16) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

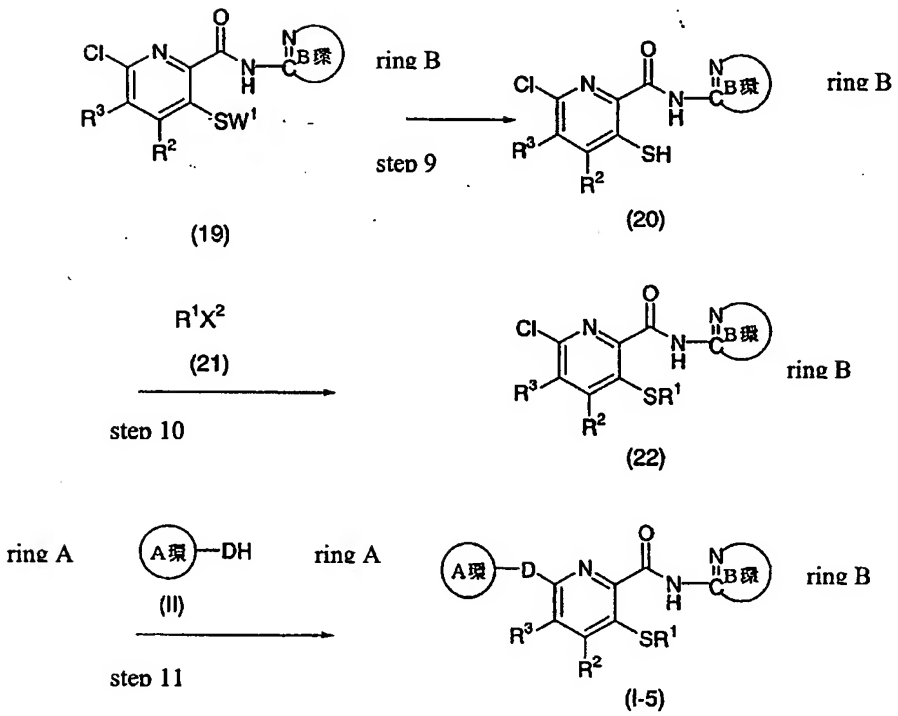
(Step 8).

This step comprises a process wherein the compound in accordance with this invention (I-4) is produced by reacting carboxylic acid derivative (16) obtained in the said step 7 and the said compound (2).

Reaction which is used in this step is the so-called amide bond forming reaction, and reaction conditions such as for example are similar to the aforesaid step 1 under equivalent quantity of the using compound, reaction temperature, the reaction time, condensing agent and a reaction assistant or the like.

The compound obtained in this way (I-4) can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography.

The compound in accordance with this invention (I-5) can be produced by following process.



(In the formula, W1 represents a thiol protecting group, X2 represents a leaving group, and other symbols are same as in the aforesaid definition).

(Step 9).

This step comprises a process wherein compound (20) is produced by eliminating the thiol protecting group from compound (19).

Elimination of the thiol protecting group in this step can be carried out by a method in accordance with literature (for example Protective Groups in Organic Synthesis, T.W. Green, Second Edition, John Wiley & Sons Co, 1991, or the like), a method in accordance with it, or a combination of these and conventional method.

The protecting group WI of thiol group is any one which is readily deprotected in this step, producing SH group.

As protecting group WI of said thiol group, substituted aralkyl group such as for example 4-methoxybenzyl group or or trityl group and the like or acyl group such as for example benzoyl group

or acetyl group and the like is nominated.

The compound (20) obtained in this way, can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, reprecipitation, solvent extraction, crystallization, chromatography and the like.

(Step 10).
This step comprises a process wherein compound (22) is produced by reacting compound (20) obtained in the said step 9 with compound (21) in the presence of base.

The compound (21) used in this step can be any compound where the X2 acts as leaving group in step 21, producing compound (22) for example a halogen atom such as fluorine atom, chlorine atom, bromine atom, iodine atom or the like, sulphonate, phosphonate and the like are nominated Among these fluorine atom, chlorine atom, iodine atom, trifluoromethane sulphonate and the like are preferred, and fluorine atom, bromine atom or iodine atom and the like is more preferred.

The reaction conditions such as for example quantity of the compound and base used in this step, the reaction time, reaction temperature, reaction solvent or the like can be the same as in the aforesaid second step.

Compound (22) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, crystallization, solvent extraction, reprecipitation, chromatography and the like.

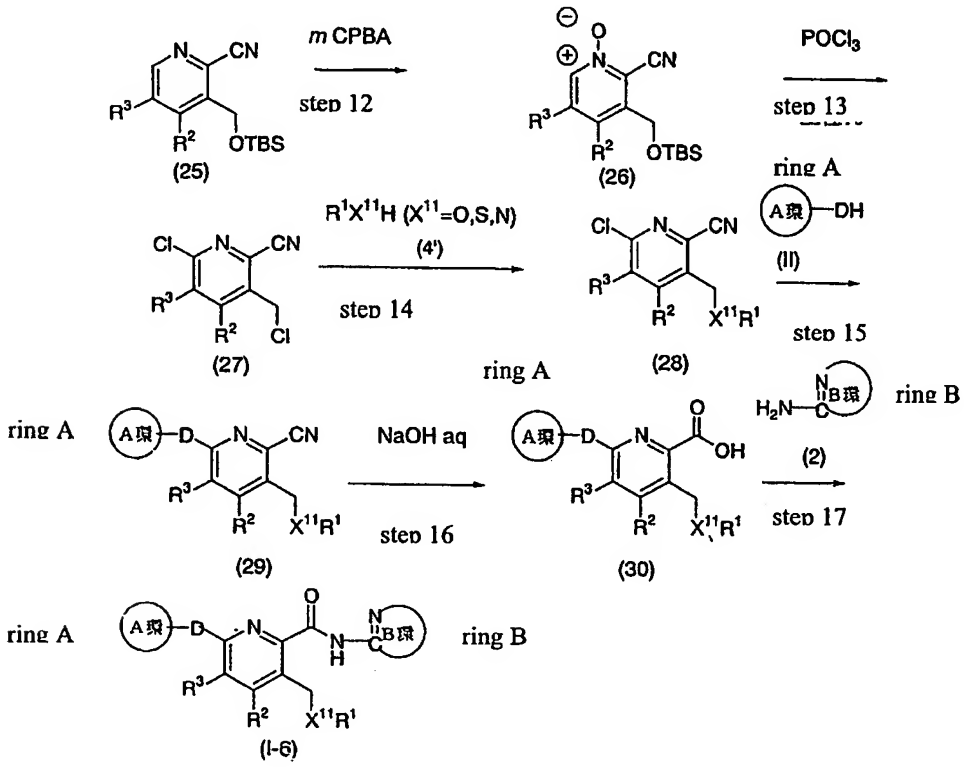
(Step 11).
This step comprises a process wherein, the compound (I-5) is produced by reacting compound (22) obtained in the said step 10 with compound (8) mentioned above in the presence of base.

The reaction conditions such as for example quantity of the compound and base used in this step, the reaction time, reaction temperature, reaction solvent or the like can be the same as in the step 2.

The compound obtained in this way (I-5) can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, crystallization,

solvent extraction, reprecipitation, chromatography and the like.

Moreover, among the compound in accordance with this invention, in the said formula (I), when XI-R1 is CH_2-CO-R1 or CH_2-S-R1, it is possible that the compound in accordance with this invention (I-6) is produced by following process.



(wherein, each symbol has the same aforesaid definitions).

(Step 12).

This step comprises a process wherein a compound (26) is produced by reacting cyanopyridine derivative (25) with mCPBA. Oxidation reaction which is used in this step can be carried out by a process in accordance with the literature (for example Tetrahedron, Vol 42, number 5, p1475-1485) or a method based on this or a combination of these with conventional methods. The quantity of mCPBA which is used is usually 0.5-1 equivalents, preferably 1-3 equivalents with respect to 1 equivalent of compound (25).

The reaction time is 10 minutes to 24 hours, preferably 30 minutes to 12 hours.

The reaction temperature is usually -20°C to boiling point of solvent temperature, preferably 0°C to boiling point of solvent temperature.

The reaction solvent to be used is any species which does not hinder the reaction, but for example chloroform, methylene chloride, 1,2-dichloroethane and the like are preferred.

Compound (26) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography.

(Step 13).
This step comprises a process wherein compound (27) is produced by reacting compound (26) obtained in the said step (12) with POC13.

The quantity of POC13 which is used is usually 0.5-100 equivalents, preferably 1-20 equivalents with respect to 1 equivalent of compound (26).

The reaction temperature is normally -20 to boiling point of solvent, preferably 20 to boiling point of solvent.

The reaction time is usually 0.5-50 hours, preferably 1-24 hours.

The reaction solvent which is used is any which does not hinder the reaction, but for example methylene chloride, chloroform, dichloromethane, acetonitrile, N,N-dimethylformamide and the like are preferred.

Compound (27) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, reprecipitation, crystallization, chromatography and the like.

(Step 14).

This step comprises a process wherein compound (28) is produced by reacting compound (27) obtained in the said step 13 with compound (12) obtained in the said step 5 in the presence of base. The reaction which is used in this step can be performed by the same method as the above-mentioned step 5 under reaction conditions such as the quantity of compound (12), the quantity of base, reaction temperature, the reaction time, reaction temperature or the like according to the method of aforesaid step 2.

Compound (28) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 15).
This step comprises a process wherein, compound (29) is produced by reacting compound (28) obtained in the said step 1 4 and the said compound (14).

The reaction conditions such as for example the reaction solvent, the quantity of the compound used in this step, the quantity of base, reaction temperature, the reaction time, or the like are the same as in the said step 2.

Compound (29) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of t well known separation and purification technique, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 16).
This step comprises a process wherein carboxylic acid compound (30) is produced by hydrolysing compound (29) obtained in the said step 15. In this step, hydrolysis by alkali is carried out.

As the alkali which is used, any can be used which can convert the cyano group of the aforesaid compound (29) into a carboxyl group, but among these sodium hydroxide aqueous solution, potassium hydroxide, barium hydroxide, lithium hydroxide and the like are preferred, and sodium hydroxide aqueous solution, potassium hydroxide aqueous solution and the like are more preferred.

The amount of alkali to use differs depending on the compound and kind of solvent, and other reaction conditions, but it is usually 1-100 equivalents, preferably 1-30 equivalents with respect to 1 equivalent

of compound (29).

The reaction temperature is usually 0 degrees to the boiling point of the solvent, preferably 50-100 degrees.

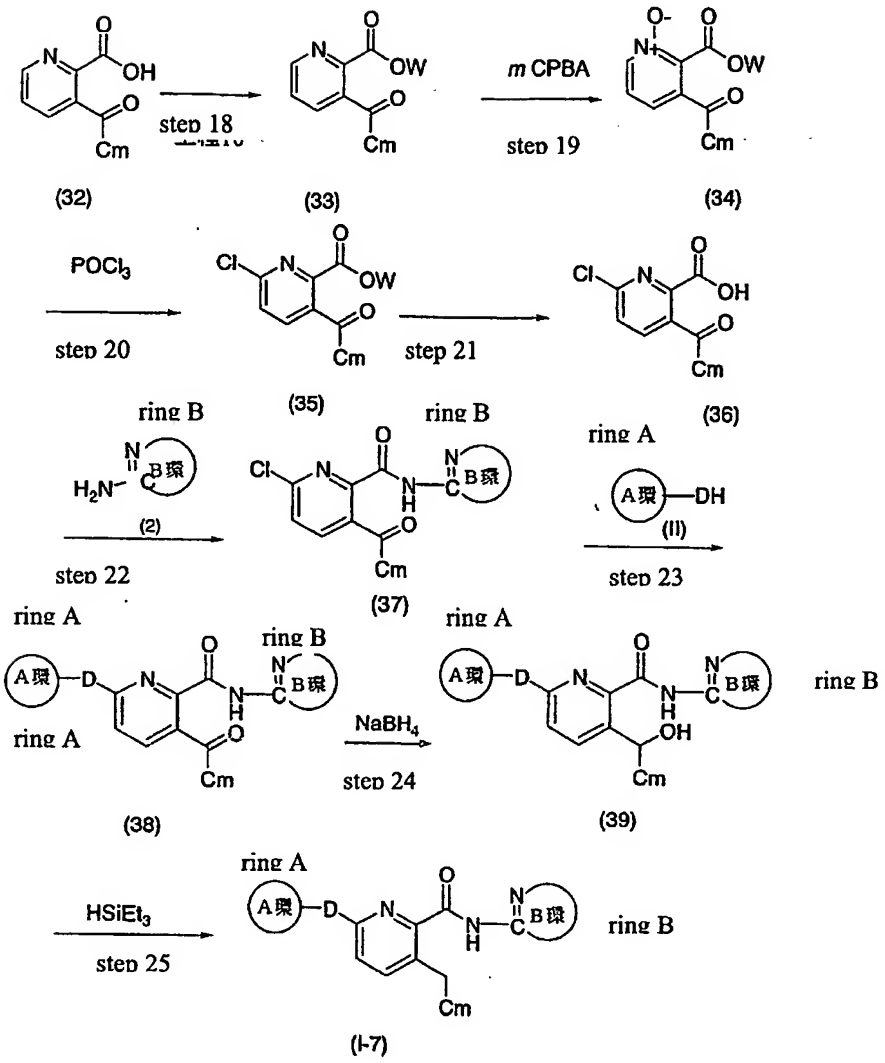
The reaction time is usually from 30 minutes to 50 hours, preferably 1-24 hours.

The reaction solvent used is preferably methanol, ethanol, isopropanol, dioxane, dimethoxyethane, ethylene glycol and the like, more preferred are ethanol, isopropanol, dioxane and the like.

Compound (30) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation purification technique, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 17).
This step is a process to produce compound (31) by reacting the carboxylic acid compound (30) obtained in the aforesaid step 16 with compound (2). This step can be carried out by using amide bond forming reaction same as in step 1, 8, as described above and it can carry out by the method according to the literature (for example, basis and practice of peptide synthesis, Nobuo Izumiya, Comprehensive Organic Synthesis, Vol. 6, Pergamon Press, 1991), a method based on this, or a combination of these with conventional method. The reaction conditions such as for example the quantity of compound (2) used, the reaction solvent, reaction temperature or the like are similar to amide bond forming reaction as described above, step 1, 8. Compound (31) obtained in this way can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

The compound (I-7) of compound (I) in accordance with this invention where XI-R1 is $-CH_2$-Cm-R1 can be produced using the following process.
(Here, Cm is a divalent saturated hydrocarbons group of 2-5C, and 1 of the carbon atoms in said divalent saturated hydrocarbons group may be replaced by nitrogen atom, oxygen atom or sulfur atom, and R1 is same as in the aforesaid definition)



(wherein, each symbol has the same aforesaid definitions).

(Step 18).

This step comprises a process wherein compound (33) is produced by introducing a protecting group into the carboxyl group of compound (32). The method of introducng protecting group of carboxyl group, is the same method as in for example the aforesaid step 4, and it can be carried out in accordance with literature (for example Protective Groups in Organic Synthesis, T.W. Green, Second

Edition, John Wiley & Sons Co, 1991, or the like), method in accordance with it or a combination of these and conventional method.

Compound (33) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 19).
This step comprises a process wherein compound (34) is produced by reacting compound (33) obtained in the said step 1 with mCPBA. It may be carried out using condition same as in the aforesaid step 12 with regard to the quantity of mCPBA used in this step, reaction temperature, the reaction solvent, other reaction conditions. The compound (34) which is obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 20).
This step comprises a process wherein compound (35) is produced by reacting compound (34) obtained in the said step 19 and POCl3.

In this step the quantity of POCl3 with respect to 1 equivalent of compound (34), reaction temperature, other reaction conditions such as for example reaction time or the like are the same as for the aforesaid step 13. Compound (35) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, reprecipitation, crystallization, chromatography and the like.

(Step 21).
This step comprises a process wherein compound (36) is produced by removing the protecting group from the carboxyl group of compound (35) obtained in the said step 20.

The removal of the protecting group W from the carboxyl group used in this step, can be carry out under the same reaction conditions as in the said step 7, or by process in accordance with literature (for example Protective Groups in Organic Synthesis, T.W. Green, Second Edition, John Wiley & Sons Co,

1991, and the like), a method in accordance with this or a combination of these with conventional method. Compound (36) obtained in this way can be subjected to next step without being isolated and purified or can be separated and purified, for example by concentration, vacuum concentration, solvent extraction, crystallization reprecipitation, chromatography and the like.

(Step 22).
This step is a process to produce compound (37) by reacting compound (36) obtained in the aforesaid step 21 with the above-mentioned compound (2).

Reaction which is used in this step may be carried out in the same way as in amide bond formation reaction such as for example the aforesaid step 1 or 8 or the like. Compound (37) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

(Step 23).
This step comprises a process wherein compound (38) is produced by reacting compound (37) obtained in the said step 22 and the said compound (14) in the presence of base. Reaction which is used in this step can be carried out by the same process as the said second step. Compound (38) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, reprecipitation, crystallization, chromatography and the like.

(Step 24).
This step comprises a process wherein compound (39) is produced by reacting compound (38) obtained in the said step 23 with NaBH4. The reaction can be carried out by process in accordance with literature (for example Comprehensive Organic Science), method in accordance with this or combination of these and conventional method in this step.

The quantity of NaBH4 which is used differs depending on compound (38) and kind of solvent, other reaction conditions used, it is usually 0.2-30 equivalents, preferably 1-10 equivalents with respect to 1 equivalent of compound (38).

The reaction temperature is usually -78°C to the boiling point of the solvent, and preferably 10-40 degrees.

The reaction time is 0.1 to 24 hours, preferably 0.2 to five hours.

The reaction solvent to be used can be any as long as it does not hinder the reaction, and for example methanol, ethanol, isopropanol, tetrahydrofuran and the like are preferred, and methanol, ethanol and the like are more preferred. Compound (39) obtained in this way can be subjected to next step without being isolated and purified or can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, reprecipitation, crystallization, chromatography and the like.

(Step 25).
This step comprises a process wherein, by reacting compound (39) obtained in the said step 24 and HSi Et3, the compound (I-7) is produced.

The reductive reaction which is used in this step can be carried out by a process in accordance with literature (J.O.C. Vol. 53, issue 22, pp. 5301-5304 (1988)), a process in accordance with this or by combining these and the conventional method.

The quantity of HSi Et3 used differs depending on kind of compound (39) and kind of solvent, other reaction conditions, but it is usually 0.5-100 equivalents, preferably 1-10 equivalents with respect to 1 equivalent of compound (39).

Usually the reaction time is 0.2-30 hours and is preferably 0.5-10 hours.

The reaction temperature is usually -10°C to the boiling point of the solvent, and is preferably 0°C to the boiling point of the solvent.

The reaction solvent to be used can be any as long as it does not hinder the reaction in this step, and for example trifluoroacetic acid is preferred. The compound obtained in this way in accordance with this invention (1-7) can be isolated and purified by using the like of well known separation and refinement means, for example concentration, vacuum concentration, solvent extraction, crystallization, reprecipitation, chromatography and the like.

Wherein, when R2 or R3 is lower alkoxy group, the hydrogen atom in the alkyl group constituting the alkoxy group may be substituted with hydroxy group or amino group, houwever, when substituted by

said hydroxy group or amino group, the introduction or elimination of protecting group of said hydroxy group or amino group is carried out in accordance with requirements in any of aforesiad step 1 to step 25.

During introduction or elimination of the said protecting group, it can be carried out by processes of the aforesaid literature (for example protective groups in organic synthesis) or the like, a process in accordance with these, or by combining these and the conventional method.

In addition, when A ring, R1 or B ring has a substituent, depending on the form of substituent, a protecting group is introduced to or eliminated from each substituent in accordance with requirements, thereby the reaction of each step can be proceeded without hindrance.

Introduction and stripping reaction of the said protecting group can be carried out by a process described in literature (for example Protective Groups in Organic Synthesis, T.W. Green, Second Edition, John Wiley & Sons Co, 1991, or the like), a method in accordance with it or combining these and conventional methods.

Pyridine-2-carboxamide derivative put forward by this invention can be present as pharmacologically acceptable salt, and as for the aforesaid salt can be produced in accordance with conventional method using aforesaid formula (I-1), (I-2), (I-3) (I-4), (I-5), (I-6) and (I-7) included by compound (I) in accordance with this invention.

In an embodiment, when the compound of aforesaid (I-1), (I-2), (I-3) (I-4), (I-5) (I-6) and (I-7) has a basic group derived from, for example the amino group, pyridyl group or the like within the aforesaid molecule, it is possible to convert to corresponding pharmacologically acceptable salt by treating the aforesaid compound with acid.

As the aforesaid acid addition salt, the acid addition salt for example hydrogen halide acid salt such as hydrochloride, hydrofluoric acid salt, hydrobromic acid salt, hydroiodic acid salt or the like, inorganic salt such as nitrate, perchlorate, sulfate, phosphate, carbonate or the like, lower alkyl sulfonate such as methanesulfonate, trifluoromethanesulfonate, ethanesulfonic acid salt or the like, aryl sulfonate such as benzensuplhonate, p-toluenesulfonate or the like, organic salt such as fumarate, succinate, citrate, tartrate, oxalate, maleate or the like and organic acid of amino acid such as glutamic acid salt, aspartate or the like are nominated. Moreover, when the compound of this invention is having acidic group in the said group, for example when it has carboxyl groups, it is possible to convert to the corresponding

pharmacologically acceptable salt by treating the aforesaid compound with base. As the aforesaid base addition salt, for example alkali metal salt such as sodium, potassium and the like, alkaline earth metal salt such as calcium, magnesium and the like, salt of organic base such as ammonium salt, guanidine, triethylamine, dicyclohexylamine and the like are nominated. Furthermore, the compound of this invention may be present as free compound or arbitrary hydrate or solventate of salts thereof.

In the production of agent for therapy or prevention of symptom or a disease related to type II diabetes mellitus or corresponding thereof, and the compound of formula (I) in accordance with this invention can be used in a combination of the compound of formula (I) and support material.

Of course the dose for therapy or prevention of the compound of formula (I) in accordance with this invention is altered by character of symptom to be treated, the specific compound and administration route to be selected.

Moreover, it is altered also by age, body weight and sensitivity of each patient. Generally dosage per day is about 0.001 mg to 100 mg per 1 kg in weight as the quantity of single administration or a plurality of administrations, and preferably it is about 0.01 mg to 50 mg, more preferably about 0.1 mg to 10 mg per 1 kg in weight. There is a case to be required to use the dose exceeding the range of these restriction.

As example of appropriate quantity of oral administration, as single or plurality of adminstrations of 2-4 times per day, it is at least 0.01 mg and at most 2.0 g. Preferably the range of dose is about 1.0 mg to about 200 mg in administration of once or twice a day. More preferably, the range of dose is about 10 mg to 100 mg in administration of once per day.

When intravenously administration or oral administration is used, typical administration range is about 0.001 mg to about 100 mg (preferably, about 0.01 mg to about 10 mg) of the compound of formula (I) per 1 kg in weight per day, and more preferably about 0.1 mg to 10 mg of the compound of formula (I) per 1 kg in body weight pre day.

As described above, medicinal composition includes the compound of formula (I) and pharmacologically acceptable carrier. The term "a composition" includes also active and inerts component constructed carrier (pharmacologically acceptable excipient) in addition to the one obtained by combining, complexing or agglomerating ny of 2 or more components directly or indirectly, the one obtained by the result of dissociation of one or more component or the one obtained by result of other

type action or interaction between components.

A composition containing the compound of formula (I) in an effective quantity for therapy or prevention of type II diabetes mellitus or delaying onset thereof by combining with pharmacologically permitted carrier is preferred.

Any appropriate administration route can be used in order to administer the effective dose of the compound in accordance with this invention to mammal, in particularly human. For example, orally, rectum, locally, vein, eye, lung, nose or the like can be used. As example of administrative form, there are tablet, troche, powder, suspension, solution, encapsulated formulation, cream, aerosol or the like, and tablet for oral is preferred.

In preparation of a composition for oral, any medium can be used so long as an ordinary medium for drug, and for example water, glycol, oil, alcohol, flavor additive, preservative, coloring agent or the like. When liquid composition for oral is prepared, for example suspension, elixir agent and solution are nominated, and as carrier, for example, starch, sugar, microcrystalline cellulose, diluent, granulating agent, lubricant, binding agent, disintegrating agent or the like are nominated. When solid composition for oral is prepared, for example, powder, encapsulated formulation, tablet or the like are nominated, and among these, solid composition for oral is preferred.

From ease of administration, tablet and encapsulated formulation are the most useful oral administration forms. Tablet can be coated with normal aqueous or non-aqueous technique in accordance with requirements.

In addition to the aforesaid ordinary administrative form, the compound in accordance with formula (I) is possible to be administered with release regulation means and/or delivery apparatus in accordance with, for example U.S. patent number 3,845,770, 3,916,899, 3,536,809, 3,598,123, 3,630,200 and 4,008,719.

As for the medicinal composition in accordance with this invention which is suitable for oral administration, it is nominated encapsulated formulation, cashew agent or tablet including active ingredient in a fixed quantity determined beforehand respectively as powder or granule, or as water-soluble liquid, water insoluble liquid, emulsion of oil in water type or emulsion of water in oil type It is possible that such composition is prepared using any kind of process in pharmaceutics, and all processes are included a process to biding together active ingredient and carrier formed from one or

more necessary component.

Generally composition is prepared by mixing thoroughly and also uniformly active ingredient and liquid carrier or solid carrier separated well or both of them, and thereafter, making product in suitable form in accordance with requirements. For example, tablet is prepared by compression and molding, together with one or more subcomponent in accordance with requirements. Compression tablet is prepared by compressing active ingredient in form such as powder, granule or the like freely with mixing with binding agent, lubricant, inert excipient, surface active agent or dispersant in accordance with requirements with a suitable machine. Formed tablet is prepared by forming mixture of the wet compound in powder form and diluent of inert liquid with a suitable machine.

Preferably each tablet includes active ingredient about 1 mg to 1 g, and each cashew agent or encapsulated formulation includes active ingredient about 1 mg to 500 mg.

Example of administrative form on drug of the compound of formula (I) is as follows.

Table 1

Suspension for injection (1.M.)

	mg/ml
Compound of formula (I)	10
Methyl cellulose	5.0
Tween 80	0.5
Benzyl alcohol	9.0
Benzalkonium chloride	1.0

It is made 1.0 ml by addition of water for injection.

Table 2

Tablet

	mg/tablet
Compound of formula (I)	25
Methyl cellulose	415
Tween 80	14.0
Benzyl alcohol	43.5
Magnesium stearate	2.5
	Total 500 mg

Table 3

Encapsulated formulation

	mg/capsole
Compound of formula (I)	25
Lactose powder	573.5
Magnesium stearate	1.5
	Total 600 mg

Table 4

Aerosol

	per 1 container
Compound of formula (I)	24 mg
Lecithin, NF Liq. Conc.	1.2 mg
Trichlorofluoromethane, NF	4.025 mg
Dichlorodifluoromethane, NF	12.15 g

The compound of formula (I) can be used by combining other agents used for therapy / prevention / delay of the onset of type II diabetes mellitus in addition to the disease or symptoms related to type II diabetes mellitus. The said other agents can be administered separately or simultaneously with the compound of formula (I) in usually-used administration route and dose.

When the compound of formula (I) is simultaneously used with one or more agent, a medicinal composition containing the compound of formula (I) and these other agents is preferable. Accordingly, the medicinal composition in accordance with this invention includes one or more other active ingredients in addition to the compound of formula (I). As example of active ingredient used by combining with the compound of formula (I), which may be administered separately or in a same medicinal composition, however, it is not restricted in following species.

(a) bis-guanide (for example, buformin, metformin, phenformin),
(b) PPAR agonist (for example, troglitazone, pioglitazone, nosiglitazone),
(c) Insulin,
(d) Somatostatin,
(e) α-glucosidase inhibitor (for example, Voglibose, miglitol, acarbose) and
(f) Insulin secretion promoter (for example, acetohexamide, carbutamide, chlorpropamide, glibomuride, gliclazide, glimepiride, glipizide, gliquidone, glisoxepid, glyburide, glyhexamide, glypinamide, phenbutamide, tolazamide, tolbutamide, tolcyclamide, nateglinide, repaglinide).

Weight ratio of the compound of formula (I) with respect to the 2nd active ingredient is altered in range of wide restriction, and moreover, it depends on effective dose of each active ingredient. Accordingly for example, when PPAR agonist is used by combining with the compound of formula (I), weight ratio of the compound of formula (I) with respect to PPAR agonist is generally about 1000 : 1-1 : 1000, and preferably about 200 : 1-1 : 200. Combination of the compound of formula (I) and other active ingredient is in the aforesaid range, however, in any case, effective dose of each active ingredient should be used.

Hereinafter glucokinase activated property shown by the compound represented by compound (I) in accordance with this invention and a test process thereof.

Measurement of excellent glucokinase activation action contained in the compound represented by the aforesaid formula (I) can be carried out by a process in accordance with literature (for example Diabetes, vol 45, pp. 1671-1677, 1996, or the like) or a method in accordance with it.

As far as glucokinase activity is concered, glucose-6-phosphoric acid is not directly measured, but degree of activation of glucokinase is determined by measuring the quantity of Thio-NADH formed, when glucose-6-phosphoric acid dehydrogenase, which is the reporter enzyme, forms phospho gluconolactone from glucose-6-phosphoric acid.

Recombinant human liver GK used in this assay was expressed in E.coli as FLAG fusion protein and refined with ANTIFLAG M2 AFFINITY GEL (Sigma).

The assay was carried out at 30°C using flat bottomed 96-well plate.

Assay buffer (25 mM Hepes Buffer: pH=7.2, 2 mM MgCl2, 1 mM ATP, 0.5 mM TNAD, 1 mM, dithiothreitol) 69 μl was aliquote and DMSO 1 μl was added as DMSO solution of the compound or control. Next, enzyme mixture (FLAG-GK, 20U/ml G6PDH) 20 μl cooled in ice was discharged, and thereafter, the substrate 25 mM glucose 10 μl was added, and reaction was started (the final glucose concentration= 2.5 mM).

After start of reaction, increase of absorbance of 405 nm was measured for ten minutes every 30 seconds, and increment for the first five minutes was used, and evaluation of the compound was carried out. FLAG-GK was added so that absorbance increment after five minutes became between 0.05-0.1 in the presence of 1 % DMSO.

The OD value with DMSO control was made 100 %, and the OD value in each concentration of the test compound was measured.

From the OD value of each concentration, Emax (%) and EC_{50} (μM) were calculated, and these were used as indicators of GK activation property of the compound.

The GK activation property of the compound in accordance with this invention was measured by this method. The results thereof are shown in the following Table 5.

Table 5

(GK activated property of the compounds of this invention).

Compound number	Emax (%)	EC_{50} (μM)
Production Example 1	997	0.05.
Production Example 7	1067	0.06.
Production Example 30	818	0.12.

As shown in the aforesaid Table 1, the compound in accordance with this invention has sufficient GK activated properties with Emax and EC_{50} as indicator.

Hereinafter, this invention will be further described in concrete terms by Preparation Examples and Production Examples. However, this invention is not restricted in any way by these.

Preparation Example 1.

The 10 pts. of compound of Production Example 1, heavy magnesium oxide 15 pts. and lactose 75 pts. were uniformly mixed and made into powdered drug in powdery-form or fine granular of 350 μm or less. This powder was introduced into capsule container and made into capsules.

Preparation Example 2

The 45 pts. of compound of Production Example 1, starch 15 pts., lactose 16 pts., crystalline cellulose 21 pts., polyvinyl alcohol 3 pts. and distilled water 30 pts. were uniformly mixed and thereafter, pulverised, granulated and dried, and thereafter, made into granule of a diameter size of 1410.177 μm by classification with a sieve.

Preparation Example 3

Granules were produced by the same process as in Preparation Example 2, and thereafter, calcium stearate 3 pts. was added with respect to this granule 96 pts., and tablets of a diameter of 10 mm were produced by compression-molding.

Preparation Example 4

Crystalline cellulose 10 pts. and calcium stearate 3 pts. were added with respect to granule 90 pts. obtained by process of Preparation Example 2, and made a tablet of a diameter of 8 mm by compression-molding, and thereafter, thereto was added syrup gelatin, precipitated calcium carbonate mixed suspension, and sugar-coated tablet was produced.

Thin layer chromatograph of Example was used Silicagel 60F245 (Merck) as plate and UV detector as detection method. As silica gel for column, Wakogel TM C.300 (Wako Jyunyaku) and as silica gel for reverse phase column, LC-SORB TM SP-B-ODS (Chemco) or YMC-GEL TM ODS-AQ 120-S50 (Yamamura Chemical Research) were used respectively.

Meaning of abbreviation in the following Examples are shown below.

i-Bu: isobutyl group.
n-Bu: n-butyl group.
t-Bu: t-butyl group.
Me: methyl group.
Et: ethyl group.

Ph: phenyl group.

i-Pr: isopropyl group.

n-P: n-propyl group.

$CDCl_3$: deuterated chloroform.

CD3OD: deuterated methanol.

DMSO-d_6 : heavy dimethyl sulphoxide.

The meaning of abbreviation in nuclear magnetic resonance spectrum are as follows.

s: singlet.

D: doublet.

Dd: double doublet.

t: triplet.

m: multiplet.

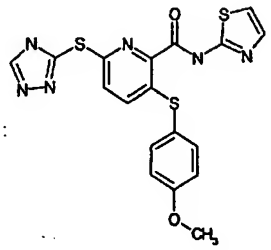
br: broad.

q: quartet.

j: coupling constant.

Hz: Hertz.

Production Example 1



Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

Aminothiazole 9.00 g (89.9 mmol), N-hydroxybenzotriazole hydrate 12-1 g (89.7 mmol) and 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride 19.0 g (99.2 mmol) were added successively to a chloroform solution (400 ml) of 3,6-dichloro-2-pyridinecarboxylic acid 14.1 g (73.0 mmol), and thereafter, it was stirred at room temperature for 24 hours. The reaction liquor was concentrated and thereafter, ethyl acetate was added to the residue and was washed with 0.2 N-

hydrochloric acid aqueous solution, water, saturated aqueous sodium bicarbonate solution and saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was crystallised from a mixed solvent of hexane-acetic acid ethyl ester (5 : 1), and thereby 3,6-dichloro-N-(thiazol-2-yl)-2-pyridinecarboxamide 12.8 g (yield = 64 %) was obtained as white solid.

Potassium carbonate 1.25 g (9.04 mmol) and 4-methoxy thiophenol 605 ml (4.87 mmol) were added to N,N-dimethylformamide solution (10 ml) of the obtained dichloro body 1.27 g (4.64 mmol), and thereafter, it was stirred at room temperature for 24 hours. Water was added to the reaction liquid and the liquid extracted with ethyl acetate and thereafter, was washed with saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 4:1 - 1:1), and 6-chloro-3-(4-methoxy-phenyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide 1.70 g (yield = 97 %) was obtained as white solid.

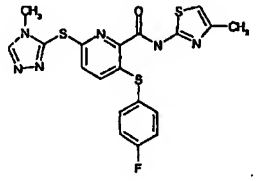
Potassium carbonate 350 mg (2.53 mmol) and 3-mercapto-1,2,4-triazole 285 mg (2.82 mmol) were added to N,N-dimethylformamide solution (10 ml) of the obtained 6-chloro derivative 705 mg (1.87 mmol) and thereafter, the mixture was heated under reflux for 35 hours. Water was added to the reaction liquor, extraction was carried out three times with chloroform, and thereafter, it was dried, and the organic layer was concentrated under reduced pressure. The obtained residue was refined by crystallization silica gel column chromatography (chloroform : methanol = 100 : 1) and mixed solvent of hexane-acetic acid ethyl ester (1 : 1), and the title compound 410 mg (yield = 50 %) was obtained as white solid.

^{1}H-NMR ($CDCl_3$) δ : 3.87 (3H, s), 6.07-7.07 (4H, m), 7.22 (1H, d, J = 8.7 Hz), 7.45 (1H, q, J = 3.6 Hz), 7.49 (2H, d, J = 9.0 Hz), 8.35 (1H, s).

ESI-MS (m/e)= 443 $(M+H)^+$.

Using the process same as in the aforesaid Production Example 1, the compounds of Production Examples 2 - 51 were obtained. Below analysis data of these compounds are shown.

Production Example 2



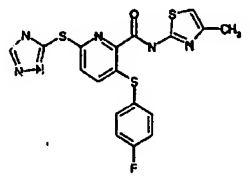
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 2 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 4-fluoro-thiophenol and 3-mercapto-4-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.42 (3H, s), 3.74 (3H, s), 6.62 (1H, s), 7.00 (1H, d, J = 9.0 Hz), 7.10 (1H, d, J = 9.0 Hz), 7.17 (2H, m), 7.53 (2H, m), 8.40 (1H, s).

ESI-MS (m/e) = 459 $(M+H)^+$.

Production Example 3



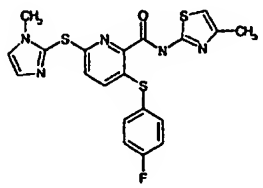
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 3 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.40 (3H, s), 6.61 (1H, s), 7.01 (1H, d, J = 9.3 Hz), 7.17-7.25 (3H, m), 7.58 (2H, m), 8.35 (1H, s).

ESI-MS (m/e) = 445 $(M+H)^+$.

Production Example 4



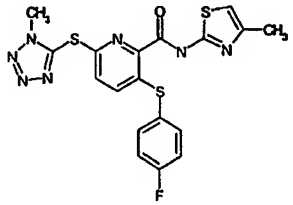
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-imidazol-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 4 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.41 (3H, s), 3.73 (3H, s), 6.60 (1H, s), 6.77 (1H, d, J = 8.7 Hz), 6.92 (1H, d, J = 8.7 Hz), 7.10-7.22 (4H, m), 7.52 (2H, m).

ESI-MS (m/e) = 458 $(M+H)^+$.

Production Example 5



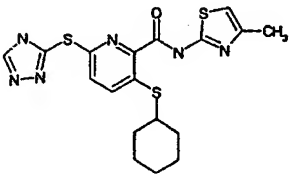
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 5 is produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 4-fluoro thiophenol and 5-mercapto-1-methyl triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.43 (3H, s), 4.12 (3H, s), 6,65(1H, s), 7.12 (1H, d, J = 9-O Hz), 7.21 (2H, m), 7.45 (1H, d, J = 9.0 Hz), 7.58 (2H, m).

ESI-MS (m/e) = 460 $(M+H)^+$.

Production Example 6



Preparation of 3-(cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

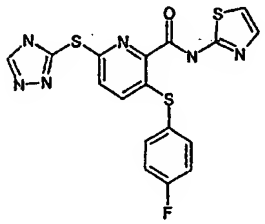
The compound of Production Example 6 can be produced using the same process as in Production

Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, cyclohexane thiol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.20-1.75 (6H, m), 1.84 (2H, m), 2.06 (2H, m), 2.36 (3H, s), 3.25 (1H, m), 6.56 (1H, s), 7.43 (1H, d, J = 8.7 Hz), 7.64 (1H, d, J = 8.7 Hz), 8.33 (1H, s).

ESI-MS (m/e) = 433 $(M+H)^+$.

Production Example 7



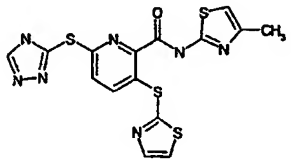
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 7 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.01 (1H, d, J = 8.7 Hz), 7.09 (1H, d, J = 3.6 Hz), 7.19 (2H, m), 7.25 (1H, d, J = 8.7 Hz), 7.50 (1H, d, J = 3.6 Hz), 7,50(2H, m), 8.35 (1H, s).

ESI-MS (m/e) = 431 $(M+H)^+$.

Production Example 8



Preparation of 3-(thiazol-2-yl-sulphanyl)-6-(4H-[1,2,41-triazol-3-yl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

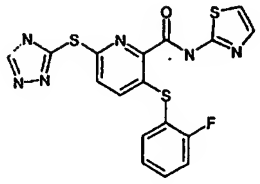
The compound of Production Example 8 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 2-mercapto-thiazole and 3-mercapto-

1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.40 (3H, s), 6.60 (1H, m), 7.30-7.36 (2H, m), 7.59 (1H, d, J = 3.6 Hz), 8.02 (1H, d, J = 3.6 Hz), 8.34 (1H, s).

ESI-MS (m/e) = 434 $(M+H)^+$.

Production Example 9



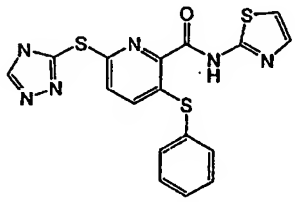
Preparation of 3-(2-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 9 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 2-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.01-7.04 (2H, m), 7.20-7.28 (3H, m), 7.46 (1H, d, J = 3.6 Hz), 7.51-7.64 (2H, m), 8.36 (1H, s).

ESI-MS (m/e) = 431 $(M+H)^+$.

Production Example 10



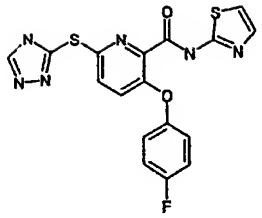
Preparation of 3-phenyl sulphanyl-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 10 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.02-7.09 (2H, m), 7.24 (1H, d, J = 8.7 Hz), 7.47-7.53 (4H, m), 7.57-7.63 (2H,

m), 8.38 (1H, s).
ESI-MS (m/e) = 413 $(M+H)^+$.

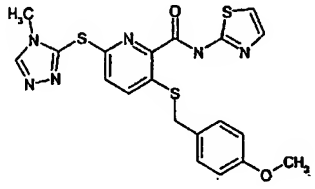
Production Example 11



Preparation of 3-(4-fluoro-phenyloxy)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 11 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid-2-aminothiazole, 4-fluorophenol and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) d : 7.04 (1H, d, J = 3.6 Hz), 7105/7.13 (4H, m), 7.24 (1H, 1d, J = 8.7 Hz), 7.46-7.51 (2H, m), 8.32 (1H, s).
ESI-MS (m/e) = 415 $(M+H)^+$.

Production Example 12

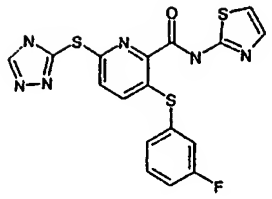


Preparation of 3-(4-methoxy-phenylmethyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 12 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-methoxybenzyl mercaptan and 3-mercapto-4-methyl-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 3.76 (3H, s), 3.79 (3H, s), 4.11 (2H, s), 6.84 (2H, d, J = 8.8 Hz), 7.01 (1H, d, J = 3.2 Hz), 7.30 (1H, d, J = 8.8 Hz), 7.32 (2H, d, J = 8.8 Hz), 7.51 (1H, d, J = 3.2Hl), 7.65 (1H, d, J = 8.8 Hz), 8.44 (1H, s).

ESI-MS (m/e) = 471 $(M+H)^+$.

Production Example 13



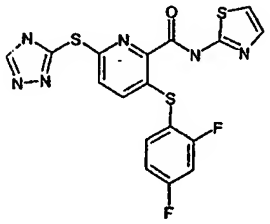
Preparation of 3-(3-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 13 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 3-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.02 (1H, d, J = 3.6 Hz), 7.05 (1H, d, J = 8.4 Hz), 7.18 (1H, td, J = 8.4Hz, 3.2 Hz), 7.24 (1H, d, J = 8.4 Hz), 7.29 (1H, ddd, J = 8.4Hz, 2.8 Hz, 2.8 Hz), 7.36 (1H, d, J = 7.6 Hz), 7.42-7.48 (2H, m), 8.35 (1H, s).

ESI-MS (m/e) = 431 $(M+H)^+$.

Production Example 14



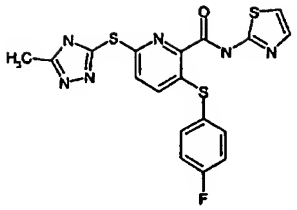
Preparation of 3-(2,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 14 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 2,4-difluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.98-7.05 (4H, m), 7.28 (1H, d, J = 8.8 Hz), 7.46 (1H, d, J = 3.6 Hz), 7.58-7.64

(1H, m), 8.36 (1H, s).
ESI-MS (m/e) = 449 $(M+H)^+$.

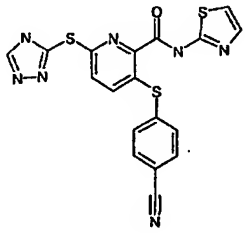
Production Example 15



Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 15 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-fluoro thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 2/58 (3H, s), 6.97 (1H, d, J = 8.4 Hz), 7.04 (1H, d, J = 3.6 Hz), 7.15-7.23 (3H, m), 7.48 (1H, d, J = 3.6 Hz), 7.54-7.58 (2H, m).
ESI-MS (m/e) = 445 $(M+H)^+$.

Production Example 16

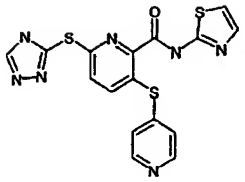


Preparation of 3-(4-cyano-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 16 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-cyano thiophenol and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 7.06 (1H, d, J = 3.6 Hz), 7.11 (1H, d, J = 8.8 Hz), 7.30 (1H, d, J = 8.3 Hz), 7.49

(1H, d, J = 3-6 Hz), 7.65 (2H, d, J = 8.8 Hz), 7.73 (2H, d, J = 8.3 Hz), 8.40 (1H, s).
ESI-MS (m/e) = 438 $(M+H)^+$.

Production Example 17

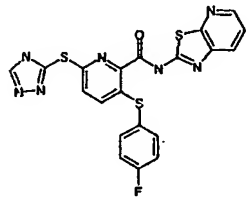


Preparation of 3-(pyridine-4-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 17 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-mercapto-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.09 (1H, d, J = 3.6 Hz), 7.28-7.35 (2H, m), 7.43 (2H, d, J = 6.0 Hz), 7.51 (1H, d, J = 3.6 Hz), 8.39 (1H, s), 8.62 (2H, d, J = 6.0 Hz).
ESI-MS (m/e) = 414 $(M+H)^+$.

Production Example 18



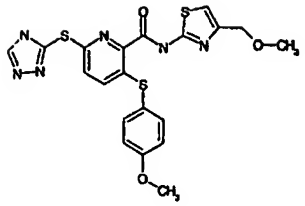
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 18 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazolo [5,4-b] pyridine, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.00 (1H, d, J = 8.8 Hz), 7.16-7.20 (2H, m), 7.25 (1H, d, J = 8.8 Hz), 7.37-7.41 (1H, m), 7.55-7.58 (2H, m), 8.02 (1H, d, J = 8.4 Hz), 8.42 (1H, s), 8.51 (1H, d, J = 4.4 Hz).

ES1-MS (m/e) = 482 $(M+H)^+$.

Production Example 19



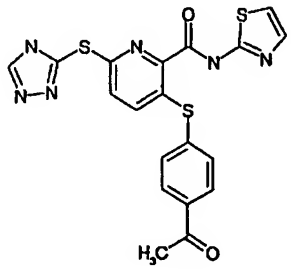
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 19 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridine carboxylic acid, 2-amino-4-methoxymethyl-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.43 (3H, s), 3.86 (3H, s), 4.51 (2H, s), 6.92 (1H, s), 6.96-7.02 (3H, m), 7.22 (1H, d, J = 8.7 Hz), 7.49 (2H, d, J = 8.7 Hz), 8.35 (1H, s).

ESI-MS (m/e) = 487 $(M+H)^+$.

Production Example 20



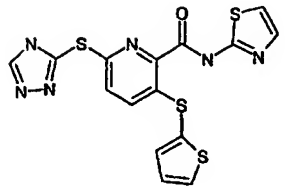
Preparation of 3-(4-acetyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 20 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-acetylthio phenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.65 (3H, s) 7.05 (1H, q, J = 3-6 Hz), 7.10 (1H, d, J = 8.4 Hz), 7.25 (1H, d, J =

8.4 Hz), 7.47 (1H, d, J = 3-6 Hz), 7.65 (2H, d, J = 8.6 Hz), 8.01 (2H, d, J = 8.6 Hz), 8.36 (1H, s).
ESI-MS (m/e) = 455 $(M+H)^+$.

Production Example 21

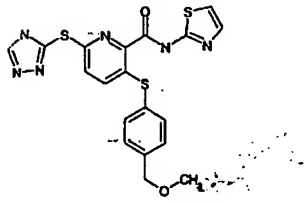


Preparation of 3-(thiophen-2-yl -sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 21 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 2-mercapto-thiophene and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.01 (1H, d, J = 3.2 Hz), 7.06 (1H, d, J = 8.8 Hz), 7.16 (1H, dd, J = 3.6, 5.2 Hz), 7.26 (1H, d, J = 8.8 Hz), 7.35 (1H qd, J = 1.2, 3.6 Hz), 7.43 (1H, q, J = 3.2 Hz), 7.60 (1H, dd, J = 1.2, 5.2 Hz), 8.35 (1H, s).
ESI-MS (m/e) = 419 $(M+H)^+$.

Production Example 22



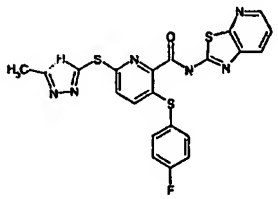
Preparation of 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 22 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-aminothiazole, 4-methoxymethyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.46 (3H, s), 4.50 (2H, s), 7.00 (1H, d, J = 3.2 Hz), 7.02 (1H, d, J = 8.8 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.42 (1H, d, J = 3.2 Hz), 7.43 (2H, d, J = 8.0 Hz), 7.54 (2H, d, J = 8.0 Hz), 8.33 (1H, s).

ESI-MS (m/e) = 457 $(M+H)^+$.

Production Example 23



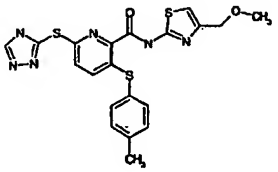
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 23 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazolo [5,4-b] pyridine, 4-fluoro thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.54 (3H, s), 6.96 (1H, d, J = 8.8 Hz), 7.11-7.16 (2H, m), 7.17 (1H, d, J = 8.8 Hz), 7.37 (1H, dd, J = 4.8, 8.0 Hz), 7.50-7.54 (2H, m), 8.00 (1H, d, J = 8.0 Hz), 8.45 (1H, d, J = 4.8 Hz).

ESI-MS (m/e) = 496 $(M+H)^+$.

Production Example 24

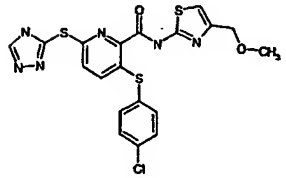


Preparation of 3-(4-methyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 24 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methoxymethyl-thiazole, 4-methylthio phenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.42 (3H, s), 3.43 (3H, s), 4.51 (2H, s), 6.91 (1H, s), 7.00 (1H, d, J = 8.8 Hz), 7.19 (1H, d, J = 8.8 Hz), 7.26 (2H, d, J = 8.4 Hz), 7.44 (2H, d, J = 8.4 Hz), 8.34 (1H, s).
ESI-MS (m/e) = 471 $(M+H)^+$.

Production Example 25

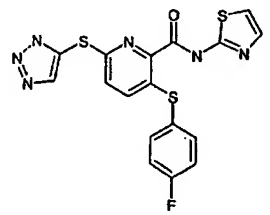


Preparation of 3-(4-chloro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 25 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methoxymethyl-thiazole, 4-chloro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.43 (3H, s), 4.50 (2H, s), 6.91 (1H, s), 6.97 (1H, q, J = 8.8 Hz), 7.20 (1H, d, J = 8.8 Hz), 7.42 (2H, q, J = 8.4 Hz), 7.49 (2H, d, J = 8.4H), 8.33 (1H, s).
ESI-MS (m/e) = 491 $(M+H)^+$.

Production Example 26



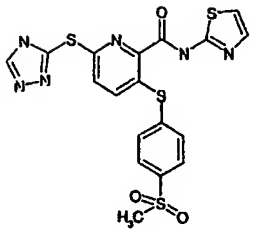
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(3H-[1,2,3] triazol-4-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 26 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methoxymethyl-thiazole, 4-fluoro thio phenol and 4-mercapto-1,2,3-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.66 (1H, d, J = 8.8 Hz), 6.72 (1H, d, J = 8.8 Hz), 6.86 (1H, d, J = 4.0 Hz), 6.89-6.94 (2H, m), 7.25 (1H, d, J = 4.0 Hz), 7.27-7.30 (2H, m), 7.72 (1H, s),

ESI-MS (m/e) = 431 $(M+H)^+$.

Production Example 27



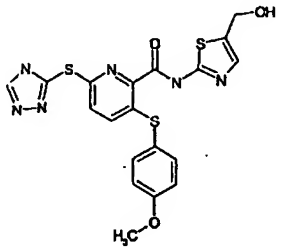
Preparation of 3-(4-methylsulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 27 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-methylsulfonyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.12 (3H, s), 7.05 (1H, d, J = 3.6 Hz), 7.11 (1H, d, J = 8.8 Hz), 7.28 (1H, d, J = 8.8 Hz), 7.48 (1H, d, J = 3.6 Hz), 7.74 (2H, d, J = 8.0 Hz), 8.00 (2H, d, J = 8.0 Hz) 8.39 (1H, s).

ESI-MS (m/e) = 491 $(M+H)^+$.

Production Example 28



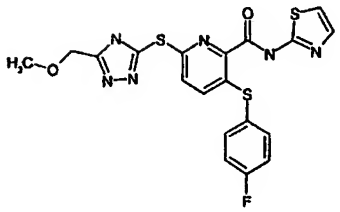
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-hydroxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 28 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-hydroxymethyl-thiazole, 4-methoxy thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.86 (3H, s), 4.78 (2H, s), 6.99 (2H, d, J = 8.8 Hz), 7.02 (1H, d, J = 8.8 Hz), 7.18

(1H, d, J = 8.8 Hz), 7.35 (1H, s), 7.46 (2H, d, J = 8.8 Hz), 8.39 (1H, s).
ESI-MS (m/e) = 473 $(M+H)^+$.

Production Example 29

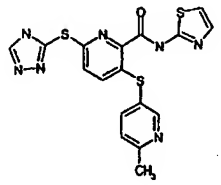


Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(5-methoxymethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 29 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole-4-fluoro thiophenol and 3-mercapto-5-methoxymethyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 3.50 (3H, s), 4.76 (2H, s), 6.98 (1H, d, J = 8.8 Hz), 7.03 (1H, d, J = 3.2 Hz), 7.14-7.22 (3H, m), 7.48 (1H, d, J = 3.2 Hz), 7.54-7.57 (2H, m).
ESI-MS (m/e) = 475 $(M+H)^+$.

Production Example 30



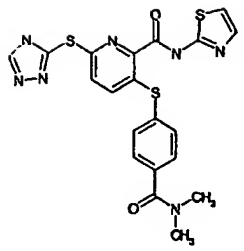
Preparation of 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 30 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR (DMSO-d_6) δ : 2.51 (3H, s), 7.17 (1H, d, J = 8.8 Hz), 7.21 (1H, d, J = 8.8 Hz), 7.35 (1H, d, J = 3.6 Hz), 7.36 (1H, d, J = 8.8 Hz), 7.57 (1H, d, J = 3.6 Hz), 7.83 (1H, dd, J = 2.4, 8.8 Hz), 8.53 (1H, d,

J = 2.4 Hz), 8.72 (1H, s).
ESI-MS (m/e)= 428 (M+H)

Production Example 31



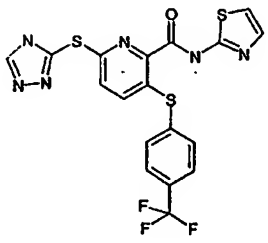
Preparation of 3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 31 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylcarbamoyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.02 (3H, s), 3.15 (3H, s), 7.04 (1H, d, J = 3.6 Hz), 7.06 (1H, d, J = 8.8 Hz), 7.23 (1H, d, J = 8.8 Hz), 7.49 (1H, d, J = 3.6 Hz), 7.50 (2H, d, J = 8.4 Hz), 7.61 (2H, d, J = 8.4 Hz), 8.39 (1H, s).

ESI-MS (m/e) = 484 $(M+H)^+$.

Production Example 32



Preparation of 3-(4-trifluoromethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

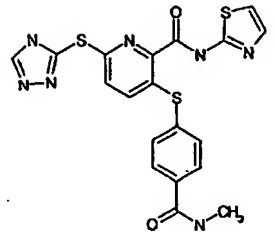
The compound of Production Example 32 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-trifluoromethylthio phenol and 3-mercapto-

1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.04 (1H, d, J = 3.6 Hz) 7.06 (1H, d, J = 8.8 Hz), 7.26 (1H, d, J = 8.8 Hz), 7,47 (1H, d, J = 3.6 Hz), 7.66-7.74 (4H, m), 8.38 (1H, s).

ESI-MS (m/e) = 481 $(M+H)^+$.

Production Example 33



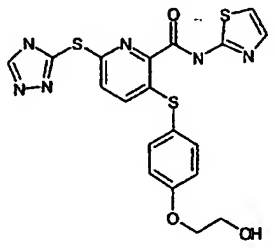
Preparation of 3-(4-methylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 33 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-methylcarbamoyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.00 (3H, d, J = 4.8 Hz), 7.02 (1H, d, J = 8.8 Hz), 7.05 (1H, d, J = 3.6 Hz), 7.20 (1H, d, J = 8.8 Hz), 7.47 (1H, d, J = 3.6 Hz), 7.59 (2H, d, J = 8.4 Hz), 7.81 (2H, d, J = 8.4 Hz), 8.32 (1H, s).

ESI-MS (m/e) = 470 $(M+H)^+$.

Production Example 34



Preparation of 3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

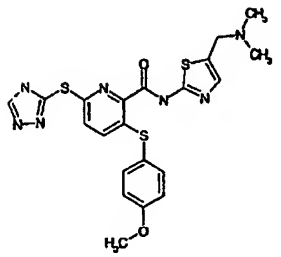
The compound of Production Example 34 can be produced using the same process as in Production

Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-hydroxyethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.97 (2H, m), 4.13 (2H, m), 7.00-7.11 (4H, m), 7.23 (1H, d, J = 9.0 Hz), 7.46-7.54 (3H, m), 8.36 (1H, s).

ESI-MS (m/e) = 473 $(M+H)^+$.

Production Example 35



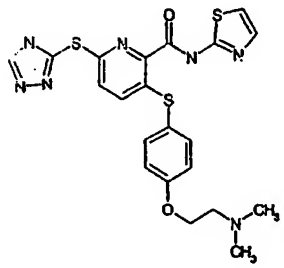
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-dimethylaminomethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 35 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-5-dimethylaminomethyl thiazole, 4-methoxy thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.32 (6H, s), 3.70 (2H, s), 3.85 (3H, s), 6.97 (2H, d, J = 8.8 Hz), 7.00 (1H, d, J = 8.5 Hz), 7.19 (1H, d, J = 8.5 Hz), 7.26 (1H, s), 7.46 (2H, d, J = 8.8 Hz), 8.31 (1H, s).

ESI-MS (m/e)= 500 $(M+H)^+$.

Production Example 36



Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-

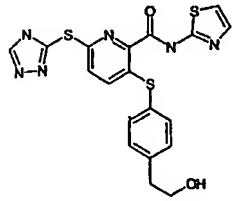
N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 36 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylaminoethyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.40 (6H, s), 2.82 (2H, t, J = 5.6 Hz), 4.13 (2H, t, J = 5.6 Hz), 6.95-7.05 (4H, m), 7.21 (1H, d, J = 8.7 Hz), 7.42-7.50 (3H, m), 8.36 (1H, s).

ESI-MS (m/e) = 500 $(M+H)^+$.

Production Example 37



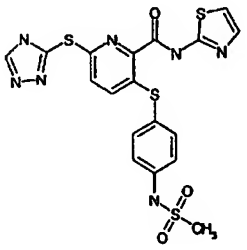
Preparation of 3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 37 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-hydroxyethyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.93 (2H, m), 3.90 (2H, m), 7.04-7.10 (2H, m), 7.23 (1H, d, J = 9.0 Hz), 7.36 (2H, d, J = 7.8 Hz), 7.48-7.56 (3H, m), 8.34 (1H, s).

ESI-MS (m/e) = 457 $(M+H)^+$.

Production Example 38



Preparation of 3-(4-methyl sulphamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-

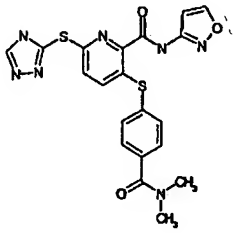
(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 38 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using .3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole-4-methyl sulphamoyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.97 (3H, s), 6.98 (1H, d, J = 3.6 Hz), 7.21-7.25 (3H, m), 7.30-7.50 (4H, m), 8.28 (1H, s).

ESI-MS (m/e) = 505 $(M)^+$.

Production Example 39



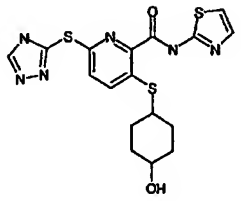
Preparation of 3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 39 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-oxazole, 4-dimethylcarbamoyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.01 (3H, s), 3.15 (3H, s), 6.99 (1H, d, J = 8.8 Hz), 7.19 (1H, d, J = 8.8 Hz), 7.25 (1H, q, J = 1.6 Hz), 7.48 (2H, d, J = 8.1 Hz), 7.56 (2H, d, J = 8.1 Hz), 8.31 (1H, d, J = 1.6 Hz), 8.41 (1H, s).

ESI-MS (m/e) = 468 $(M+H)^+$.

Production Example 40



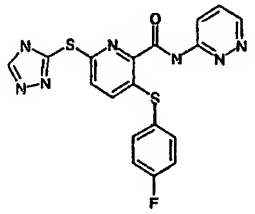
Preparation of 3-(4-hydroxy-cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 40 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-mercapto-cyclohexanol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.30-1.60 (4H, m), 1.90-2.15 (4H, m), 3.10-3.22 (1H, m), 3.60-3.70 (1H, m), 6.99 (1H, d, J = 3.6 Hz), 7.40 (1H, d, J = 8.8 Hz), 7.43 (1H, d, J = 3.6 Hz), 7.61 (1H, d, J = 8.8 Hz), 8.32 (1H, s).

ESI-MS (m/e) = 435 $(M+H)^+$.

Production Example 41



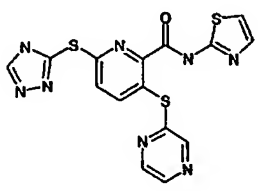
Preparation of 3-(4-fluoro-phenyl sulphanyl)-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridazine-3-yl)-2-pyridinecarboxamide

The compound of Production Example 41 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-pyridazine, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.96 (1H, d, J = 9.2 Hz), 7.12-7.16 (2H, m), 7.19 (1H, d, J = 9.2 Hz), 7.50-7.55 (3H, m), 8.41 (1H, s), 8.65 (1H, d, J = 9.2 Hz), 8.85 (1H, d, J = 4.8 Hz).

ESI-MS (m/e) = 426 $(M+H)^+$.

Production Example 42



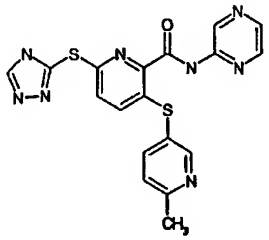
Preparation of 3-(pyrazine-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 42 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 2-mercapto-pyrazine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 7.02 (1H, d, J = 3.6 Hz), 7.39 (1H, d, J = 8.8 Hz), 7.45 (1H, d, J = 3.6 Hz), 7.68 (1H, d, J = 8.8 Hz), 8.38 (1H, s), 8.44-8.46 (2H, m), 8.70 (1H, d, J = 1.6 Hz).

ESI-MS (m/e)= 415 $(M+H)^+$.

Production Example 43



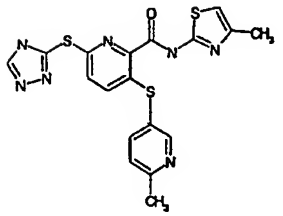
Preparation of 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 43 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-pyrazine, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.64 (3H, s), 6.96 (1H, q, J = 8.3 Hz), 7.17 (1H, q, J = 8.3 Hz), 7.28 (1H, d, J = 8.1 Hz), 7.77 (1H, dq, J = 8.1, 2.2 Hz), 8.29 (1H, dd, J = 2.6, 1.5 Hz), 8.35 (1H, d, J = 2.6 Hz), 8.41 (1H, s), 8.61 (1H, d, J = 2.2 Hz), 9.68 (1H, q, J = 1.5 Hz).

ESI-MS (m/e) = 423 $(M+H)^+$.

Production Example 44



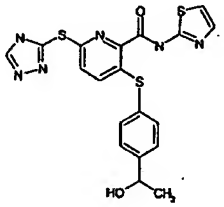
Preparation of 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 44 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methyl-thiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.39 (3H, s), 2.63 (3H, s), 6.58 (1H, s), 6.99 (1H, d, J = 8.8 Hz), 7.20-7.30 (2H, m), 7.74 (1H, d, J = 8.0 Hz), 8.32 (1H, s), 8.62 (1H, s).

ESI-MS (m/e) = 442 $(M+H)^+$.

Production Example 45



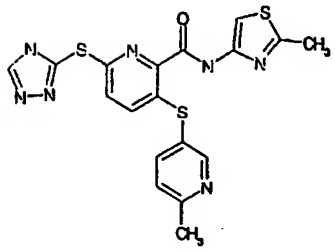
Preparation of 3-[4-(1-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 45 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-(1-hydroxyethyl) thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.52 (3H, d, J = 6.4 Hz), 4.97 (1H, q, J = 6.4 Hz), 7.03 (1H, d, J = 8.4 Hz), 7.06 (1H, d, J = 3.6 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.47 (2H, d, J = 8.0 Hz), 7.48 (1H, d, J = 3.6 Hz), 7.52 (2H, d, J = 8.0 Hz), 8.34 (1H, s).

ESI-MS (m/e) = 457 (M+H).

Production Example 46



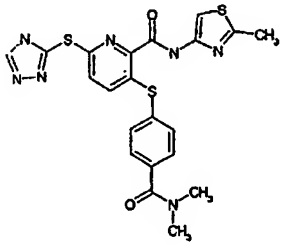
Preparation of 3-(6-methyl-pyridin-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridinecarboxamide

The compound of Production Example 46 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.63 (3H, s), 2.72 (3H, s), 6.96 (1H, d, J = 8.4 Hz), 7.19 (1H, d, J = 8.1 Hz), 7.27 (1H, d, J = 8.4 Hz), 7.68 (1H, s), 7.76 (1H, dd, J = 8.4, 2.2 Hz), 8.26 (1H, s), 8.59 (1H, d, J = 2.2 Hz).

ESI-MS (m/e) = 442 $(M+H)^+$.

Production Example 47



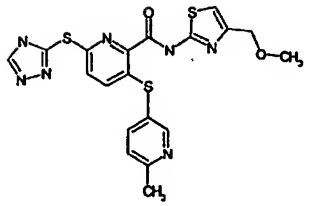
Preparation of 3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridinecarboxamide

The compound of Production Example 47 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methylthiazol, 4-dimethylcarbamoyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.69 (3H, s), 3.00 (3H, s), 3.14 (3H, s), 6.95 (1H, d, J = 8.8 Hz), 7.11 (1H, d, J = 8.8 Hz), 7,45 (2H, d, J = 8.1 Hz), 7.56 (2H, d, J = 8.1 Hz), 7.64 (1H, s), 8.29 (1H, s).

ESI-MS (m/e)= 498 (M+H) +.

Production Example 48



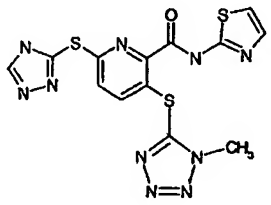
Preparation of 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 48 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methoxymethyl-thiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.62 (3H, s), 3.44 (3H, s), 4.51 (2H, s), 6.91 (1H, s), 6.93 (1H, d, J = 8.4 Hz), 7.19 (1H, d, J = 8.4 Hz), 7.26 (1H, d, J = 8.0 Hz), 7.77 (1H, dd, J = 8.0 Hz, 2.4 Hz), 8.35 (1H, s), 8.61 (1H, d, J = 2.4 Hz).

ESI-MS (m/e) = 472 (M+H).

Production Example 49



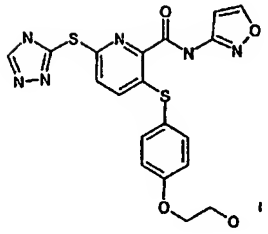
Preparation of 3-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 49 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 5-mercapto-1-methyl-1,2,4-triazole and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 4.11 (3H, s), 7.11 (1H, d, J = 3.2 Hz), 7.38 (1H, q, J = 8.3 Hz), 7.36 (1H, d, J = 8.8 Hz), 7.52 (1H, d, J = 3.2HI), 8.42 (1H, s).

ESI-MS (m/e) = 419 (M+H).

Production Example 50



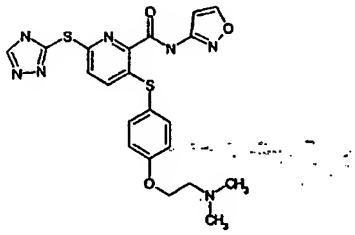
Preparation of 3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 50 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-aminooxazole, 4-hydroxyethyl thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3,91 (2H, t, J = 4.6 Hz), 4.05 (2H, t, J = 4.6 Hz), 6.91 (1H, d, J = 8.8 Hz), 6.92 (2H, d, J = 8.4 Hz), 7.11 (1H, d, J = 8.8 Hz), 7.22 (1H, d, J = 1.5 Hz), 7.39 (2H, q, J = 8.4 Hz), 8.25 (1H, d, J = 1.5 Hz), 8.29 (1H, s).

ESI-MS (m/e) = 457 $(M+H)^+$.

Production Example 51



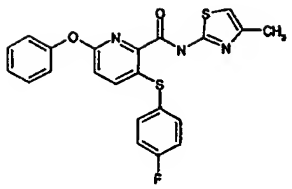
Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 51 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-oxazole, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.43 (6H, s), 2,85 (2H, t, J = 5.5 Hz), 4.12 (2H, t, J = 5.5 Hz), 6.90 (2H, d, J = 8.8 Hz), 6.93 (1H, d, J = 8.8 Hz), 7.15 (1H, d, J = 8.8 Hz), 7.24 (1H, s), 7.38 (2H, d, J = 8.8 Hz), 8.30 (1H,

s), 8.38 (1H, s).
ESI-MS (m/e) = 484 $(M+H)^+$.

Production Example 52



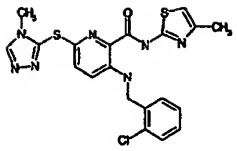
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-phenoxy-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

Phenol 135 mg (1.43 mmol) and cesium carbonate 540 mg (1.66 mmol) were added to N,N-dimethylformamide solution (3 ml) of 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide 84 mg (0.292 mmol) obtained using the same process as in Production Example 1, and thereafter, it was stirred at 120°C for 24 hours. A 1 N-sodium hydroxide aqueous solution was added to the reaction liquor, and thereafter, extraction was carried out with ethyl acetate. The organic layer was washed with water and saturated aqueous sodium chloride solution and was dried, and concentration was carried out under reduced pressure. The obtained residue was refined using thin layer silica gel chromatography (hexane : ethyl acetate = 4:1), and 3-chloro-6-phenoxy-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide 61 mg (yield = 61 %) was obtained as a white solid.

Potassium carbonate 80 mg (0.579 mmol) and 4-fluoro thiophenol 20 ml (0.188 mmol) were added to N,N-dimethylformamide solution (2 ml) of the obtained 3-chloro derivative 23 mg (0.0799 mmol), and thereafter, the mixture was stirred at 100°C for 16 hours. Water was added to the reaction liquid, the liquid was extracted with ethyl acetate and thereafter, was washed with saturated aqueous sodium chloride solution. The residue obtained after drying and concentration was refined using thin layer silica gel chromatography (hexane : ethyl acetate = 4:1), and the title compound 11 mg (yield = 32 %) was obtained as white solid.
^{1}H-NMR ($CDCl_3$) d : 2.37 (3H, s), 6.58 (1H, s), 6.90 (1H, d, J = 9.0 Hz), 7.10-7.23 (6H, m), 7.46 (1H, qq, J = 7.8, 7.8 Hz), 7.62 (2H, m).
ESI-MS (m/e)= 438 $(M+H)^+$.

Using process same as in the aforesaid Production Example 52, the compound of Production Example 53 was obtained. Below analysis data of the compound are shown.

Production Example 53



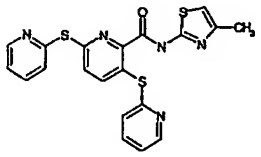
Preparation of 3-(2-chloro-phenylmethyl-amino)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 53 can be produced using the same process as in Production Example 52, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide obtained using the same process as in Production Example 1, 2-chloro-benzylamine and 3-mercapto-4-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.41 (3H, s), 3.73 (3H, s), 4.55 (2H, d, J = 6.0 Hz), 6.58 (1H, s), 6.92 (1H, d, J = 9.3 Hz), 7.20-7.45 (5H, m), 8.32 (1H, s), 8.72 (1H, m).

ESI-MS (m/e) = 472,474 $(M+H)^+$.

Production Example 54



Preparation of 3,6-bis-(pyridine-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

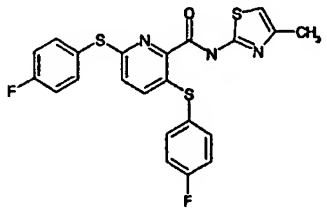
2-mercaptopyridine 24 mg (0.205 mmol) and potassium carbonate 68 mg (0.492 mmol) were added to N,N-dimethylformamide solution (2 ml) of 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide 43 mg (0.149 mmol) obtained using the same process as in Production Example 1, and thereafter, it was stirred at 100°C for 15 hours. Water was added to the reaction liquid, the liquid was extracted with ethyl acetate and thereafter, was washed with saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using thin layer silica gel chromatography (chloroform : methanol = 20:1), and the title compound 15 mg (yield = 23 %) was obtained as yellow solid.

^{1}H-NMR ($CDCl_3$) δ : 2.39 (3H, s), 6.58 (1H, s), 7.20-7.30 (2H, m), 7.40 (1H, d, J = 8.6 Hz), 7.46 (1H, br. d, J = 8.1 Hz), 7.52-7.75 (4H, m), 8.55-8.65 (2H, m).

ESI-MS (m/e)= 438 $(M+H)^+$.

Using the same process as in the aforesaid Production Example 54, the compound of Production Examples 55 - 57 were obtained. Below analysis data of these compounds are shown.

Production Example 55



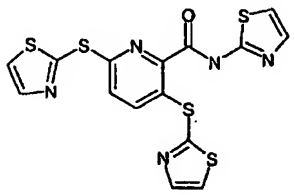
Preparation of 3,6-bis-(4-fluoro-phenyl sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 55 can be produced using the same process as in Production Example 54, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide using the same process as in Production Example 1 and 4-fluoro thiophenol obtained.

^{1}H-NMR ($CDCl_3$) δ : 2.41 (3H, s), 6.59 (1H, s), 6.77 (1H, d, J = 9.0 Hz), 6.88 (1H, d, J = 9.0 Hz), 7.09-7.20 (4H, m), 7.49-7.60 (4H, m).

ESI-MS (m/e) = 472 $(M+H)^+$.

Production Example 56



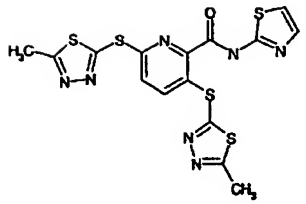
Preparation of 3,6-bis-(thiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 56 is produced using the same process as in Production Example 54, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide obtained using the same process as in Production Example 1 and 2-mercapto-thiazole.

^{1}H-NMR ($CDCl_3$) δ : 7.06 (1H, d, J = 3.6 Hz), 7.27 (1H, d, J = 8.8 Hz), 7.37 (1H, d, J = 8.8 Hz), 7.54 (1H, d, J = 3.6 Hz), 7.59 (1H, d, J = 3.6 Hz), 7.61 (1H, d, J = 3.6 Hz), 7.98 (1H, d, J = 3.6 Hz), 8.02 (1H, d, J = 3.6 Hz).

ESI-MS (m/e) = 436 $(M+H)^+$.

Production Example 57



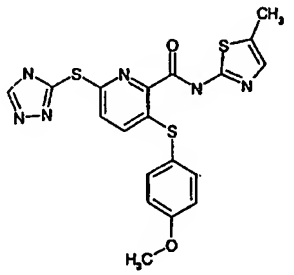
Preparation of 3,6-bis-(5-methyl-[1,3,4] thiadiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 57 is produced using the same process as in Production Example 54, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-N-(4-methyl-thiazol-2-yl)-2-pyridinecarboxamide obtained using the same process as in Production Example 1 and 2-mercapto-5-methyl-1,3,4-thiazole.

^{1}H-NMR ($CDCl_3$) δ : 2.86 (3H, s), 2.91 (3H, s), 7.07 (1H, d, J = 3.6 Hz), 7.44 (1H, d, J = 8.8 Hz), 7.52 (1H, d, J = 3.6 Hz), 7.64 (1H, d, J = 8.3 Hz).

ESI-MS (m/e) 466 $(M+H)^+$.

Production Example 58



Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-methyl-thiazol-2-yl)-2-pyridinecarboxamide

Concentrated sulfuric acid 0.441 ml (8.27 mmol) under room temperature was added dropwise to dichloromethane suspension (35 ml) of magnesium sulfate 3.86 g (32.2 mmol) and on completion of the dropwise addition, it was stirred at room temperature for 20 minutes. Thereafter, 3,6-dichloro-2-pyridinecarboxylic acid 750 mg (3.91 mmol) and dichloromethane (10 ml) solution of tert-butyl alcohol 3.84 ml (40.2 mmol) were added to the reaction liquor at room temperature and thereafter, the

mixture was stirred vigorously at room temperature for 15 hours. Aqueous solution (40 ml) of sodium carbonate 3.0 g was added dropwise to the reaction liquor under ice cooling, and it was stirred till the reaction liquor became a uniform solution. The reaction liquor was extracted with chloroform, the organic layer was washed with saturated aqueous sodium chloride solution, and thereafter, it was dried, and concentration was carried out under reduced pressure. The obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 97:3) and 3,6-dichloro-2-pyridinecarboxylic acid tert-butyl 644 mg (yield = 66 %) was obtained as a white solid.

At room temperature, 4-methoxy thiophenol 0.927 ml (7.55 mmol) and potassium carbonate 1.14 g (8.26 mmol) were added to N,N-dimethylformamide solution (70 ml) of the obtained ester 1.70 g (6.86 mmol) and the mixture was stirred for one hour. Chloroform was added to the reaction liquor and was washed with saturated aqueous sodium bicarbonate solution and saturated aqueous sodium chloride solution, and thereafter, it was dried, and concentration was carried out under reduced pressure. The obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 9:1) and 6-chloro-3-(4-methoxy-phenyl sulphanyl)-2-pyridinecarboxylic acid tert-butyl 743 mg (yield = 31 %) was obtained as a colourless oily substance.

At room temperature, 3-mercapto-1,2,4-triazole 258 mg (2.55 mmol) and potassium carbonate 353 mg (2.56 mmol) were added to N,N-dimethylformamide solution (30 ml) of the obtained chloro body 451 mg (1.28 mmol), and the reaction liquor was stirred at 130°C for ten hours. Chloroform was added to the reaction liquor and was washed with saturated aqueous sodium bicarbonate solution and saturated aqueous sodium chloride solution, and thereafter, it was dried, and concentration was carried out under reduced pressure. The obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 2:1) and 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-2-pyridinecarboxylic acid tert-butyl 264 mg (yield = 49 %) was obtained as a colourless oily substance.

Trifluoroacetic acid 2.0 ml was added at room temperature to dichloromethane solution (5.0 ml) of the obtained ester 264 mg (0.633 mmol), the reaction liquor was stirred at room temperature for one hour 30 minutes. The reaction liquor was concentrated under reduced pressure, and 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-2-pyridinecarboxylic acid 228 mg was obtained as a straw-coloured solid.

At room temperature, 5-methylamino thiazole 3.2 mg (29 μmol), N-hydroxybenzotriazole hydrate 3.8 mg (27 μmol), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride 5.4 mg (28 μmol) were added successively to dichloromethane solution (1.0 ml) of the obtained carboxylic acid body 5.9 mg

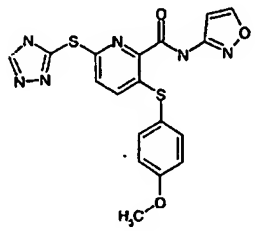
(16 μmol), and the reaction liquor was stirred at room temperature for three hours. Saturated aqueous sodium bicarbonate solution was added to the reaction liquor and extraction was carried out with chloroform. The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter, it was dried, and concentration was carried out under reduced pressure. The obtained residue was refined using silica gel column chromatography (chloroform : methanol = 95:5) and the title compound 2.0 mg (yield = 15 %) was obtained as a straw-coloured solid.

^{1}H-NMR ($CDCl_3$) d : 2.43 (3H, s), 3.86 (3H, s), 6.98 (2H, d, J = 8.4 Hz), 6.99 (1H, d, J = 8.4 Hz), 7.09 (1H, s), 7.19 (1H, d, J = 8.4 Hz), 7.47 (2H, d, J = 8.4 Hz), 8.32 (1H, s).

ESI-MS (m/e)= 457 $(M+H)^+$.

Using the process same as in the aforesaid Production Example 58, the compounds of Production Examples 59 - 65 were obtained. Below analysis data of these compounds are shown.

Production Example 59



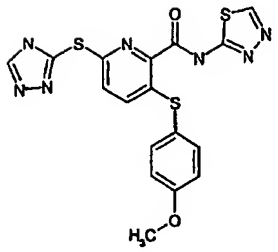
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 59 can be produced using the same process as in Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 3-amino-isoxazole.

^{1}H-NMR ($CDCl_3$) δ : 3.86 (3H, s), 6.98 (2H, d, J = 8.4 Hz), 6.99 (1H, d, J = 8.4 Hz), 7.19 (1H, d, J = 8.4 Hz), 7.30 (1H, s), 7.47 (2H, d, J = 8.4 Hz), 8.31 (1H, s), 8.41 (1H, s).

ESI-MS (m/e) = 427 $(M+H)^+$.

Production Example 60



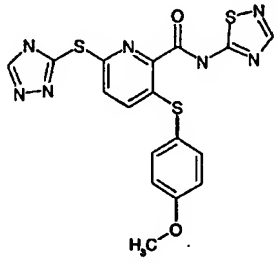
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,3,4] thiadiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 60 can be produced using Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 2-amino-1,3,4-thiadiazole.

^{1}H-NMR ($CDCl_3$) d : 3.86 (3H, s), 6.99 (2H, q, J = 8.5 Hz), 7.03 (1H, d, J = 8.4 Hz), 7.23 (1H, d, J = 8.4 Hz), 7,47 (2H, d, J = 8.5 Hz), 8.45 (1H, s), 8.85 (1H, s).

ESI-MS (m/e) = 444 $(M+H)^+$.

Production Example 61



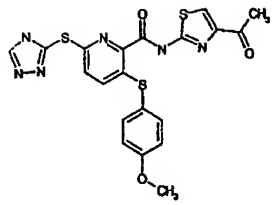
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 61 can be produced using Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 5-amino-1,2,4-thiadiazole.

^{1}H-NMR ($CDCl_3$) δ : 3.87 (3H, s), 7.00 (2H, d, J = 8.4 Hz), 7.01 (1H, d, J = 8.4 Hz), 7.20 (1H, q, J = 8.4 Hz), 7.48 (2H, d, J = 3.5 Hz), 7.80 (1H, s), 8.36 (1H, s)

ESI-MS (m/e) = 444 $(M+H)^+$.

Production Example 62



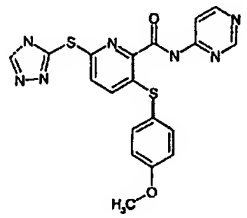
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl carbonyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 62 can be produced using the same process as in Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 4-acetyl-2-amino-thiazole.

^{1}H-NMR ($CDCl_3$) δ : 2.63 (3H, s), 3.86 (3H, s), 6.98 (1H, d, J = 8.8 Hz), 7.01 (2H, d, J = 8.8 Hz), 7.22 (1H, d, J = 8.8 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.86 (1H, s), 8.33 (1H, s).

ESI-MS (m/e) 485 $(M+H)^+$.

Production Example 63



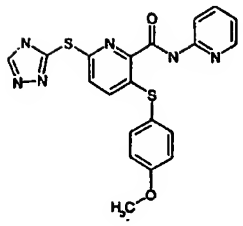
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrimidin-4-yl)-2-pyridinecarboxamide

The compound of Production Example 63 can be produced using the same process as in Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 4-amino-pyrimidine.

^{1}H-NMR ($CDCl_3$) δ : 3.86 (3H, s), 6.98 (2H, d, J = 8.8 Hz), 7.02 (1H, d, J = 8.4 Hz), 7.22 (1H, d, J = 8.4 Hz), 7.46 (2H, d, J = 8.8 Hz), 8.38 (1H, dd, J = 5.9, 0.8 Hz), 8.41 (1H, s), 8.65 (1H, d, J = 5.9 Hz), 8.93 (1H, d, J = 0.8 Hz).

ESI-MS (m/e) = 438 $(M+H)^+$.

Production Example 64



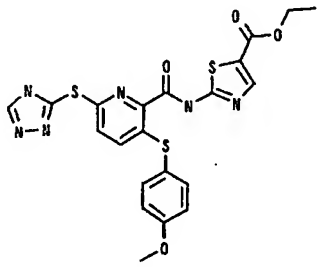
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 64 can be produced using the same process as in Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-methoxy thiophenol, 3-mercapto-1,2,4-triazole and 2-amino-pyridine.

^{1}H-NMR ($CDCl_3$) δ : 3,85 (3H, s), 6.97 (2H, d, J = 8.8 Hz), 6.99 (1H, d, J = 8.8 Hz), 7.05 (1H, dd, J = 8.5, 4.5 Hz), 7.18 (1H, d, J = 8.8 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.73 (1H, ddd, J = 8.5, 8.5, 1.5 Hz), 8.29 (1H, dd, J = 4.5, 1.5 Hz), 8.31 (1H, s), 8.41 (1H, d, J = 8.5 Hz).

ESI-MS (m/e) = 437 $(M+H)^+$.

Production Example 65



Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-ethoxycarbonyl-thiazol-2-yl)-2-pyridinecarboxamide

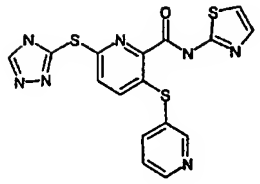
The compound of Production Example 65 can be produced using the same process as in Production Example 58, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridine carboxylic acid possible 4-methoxy thiophenol-3-mercapto-1,2,4-triazole and 2-amino-5-ethoxycarbonyl-thiazole.

^{1}H-NMR ($CDCl_3$) d : 1.37 (3H, t, J = 7.0 Hz), 3.86 (3H, s), 4.34 (2H, q, J = 7.0 Hz), 6.98 (2H, d, J =

8.8 Hz), 7.00 (1H, d, J = 8.5 Hz), 7.20 (1H, d, J = 8.5 Hz), 7.46 (2H, d, J = 8.8 Hz), 8.11 (1H, s), 8.36 (1H, s)

ESI-MS (m/e)= 515 $(M+H)^+$.

Production Example 66



Preparation of 3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

Anisole 0.40 ml (0.390 mmol) and trifluoroacetic acid 5 ml were added to 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide 152 mg (0.390 mmol) obtained using the same process as in Production Example 1, the reaction liquor was stirred at 60°C for five hours, and thereafter was stirred at room temperature overnight. The reaction liquor was concentrated under reduced pressure, and 3-thiol derivative was obtained as an orange oily substance. Ethylene glycol 62 µl (1.10 mmol), potassium carbonate 141 mg (1.02 mmol), 3-iodopyridine 114 mg (0.560 mmol) and copper iodide 5.3 mg (0.030 mmol) were added to a 2-propanol solution (3 ml) of the previously obtained 3-thiol derivative, the reaction liquor was stirred at 80 degrees overnight. The reaction liquor was filtered with cellite, and the filtrate was distributed with chloroform and water. The organic layer was washed with water and was dried, and thereafter concentrated under reduced pressure. The obtained residue was refined using thin layer silica gel chromatography (hexane : ethyl acetate = 1:1) and 6-chloro derivative 28 mg (yield = 21 %) was obtained as a straw-coloured solid.

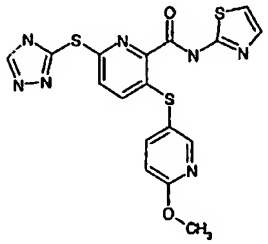
3-mercapto-1,2,4-triazole 22 mg (0.22 mol) was added to N,N-dimethylformamide solution (1 ml) of potassium t-butoxide 25 mg (0.22 mmol), thereafter, N,N-dimethylformamide solution (3 ml) of previously obtained 6-chloro derivative 28 mg (0.080 mmol) was added dropwise, and on completion of the dropwise addition, the reaction liquor was stirred at 120°C for two hours. Water was added to the reaction liquor and extraction was carried out with chloroform. The organic layer was washed with water, dried and concentrated. The obtained residue was refined using thin layer silica gel chromatography (chloroform : methanol = 9:1) and the title compound 12 mg (yield = 37 %) was obtained as a straw-coloured solid.

^{1}H-NMR ($CDCl_3$) d : 6.96 (1H, d, J = 8.8 Hz), 7.05 (1H, d, J = 3.6 Hz), 7.22 (1H, d, J = 8.8 Hz), 7.40-

7.43 (1H, m), 7.47 (1H, d, J = 3.6 Hz), 7.87-7.90 (1H, m), 8.32 (1H, s), 8.64-8.66 (1H, m), 8.70-8.71 (1H, m).
ESI-MS (m/e)= 414 $(M+H)^+$.

Using the same process as in the aforesaid Production Example 66, the compounds of Production Examples 67 - 68 were obtained. Below analysis data of these compounds are shown.

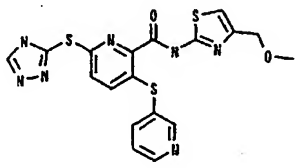
Production Example 67



Preparation of 3-(6-methoxy-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 67 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained using the same process as in Production Example 1, 6-methoxy-3-iodopyridine and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 4.00 (3H, s), 6.87 (1H, d, J = 8.7 Hz), 7.00-7.11 (2H, m), 7.26 (1H, d, J = 8.4 Hz), 7.46 (1H, d, J = 3.3 Hz), 7.77 (1H, dd, J = 2.4, 8.7 Hz), 8.35 (1H, d, J = 2.4 Hz), 8.38 (1H, s).
ESI-MS (m/e) = 444 $(M+H)^+$.

Production Example 68



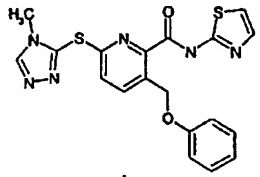
Preparation of 3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 68 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethylsulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide obtained using the same process as in Production Example 1, 3-iodopyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.49 (3H, s), 4.56 (2H, s), 6.94 (1H, s), 6.97 (1H, d, J = 8.8 Hz), 7.27 (1H, d, J = 8.8 Hz), 7.43 (1H, dd, J = 7.6Hz, 3.3 Hz), 7.93 (1H, d, J = 7.6 Hz), 8.38 (1H, s), 8.71 (1H, d, J = 4.8 Hz), 8.77 (1H, s).

ESI-MS (m/e) = 458 $(M+H)^+$.

Production Example 69



Preparation of 3-phenyloxy methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazole-2 yl)-2-pyridinecarboxamide

3-chloroperbenzoic acid 6.30 g (21.0 mmol) was added to chloroform solution (50 ml) of 2-cyano-3-tert-butyldimethylsilyloxymethyl pyridine 3.50 g (14.0 mmol) and was heated under reflux overnight. Saturated aqueous sodium bicarbonate solution was added to the reaction liquor, thereafter, extraction with chloroform was carried out, and the organic layer was washed with water, saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 2:1) and N-oxide body 1.50 g (yield = 41 %) was obtained as white solid.

A phosphorus oxychloride solution (10 ml) of the obtained N-oxide body 1.50 g (5.70 mmol) was stirred at 80°C for one hour. The reaction liquor was concentrated under reduced pressure, thereafter, saturated aqueous sodium bicarbonate solution was added to the obtained residue, extraction was carried out with chloroform, and the organic layer was washed with saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using silica gel column chromatography (hexane : ethyl acetate = 2:1) and 2-chloro-5-chloromethyl-6-cyanopyridine 625 mg (yield = 58 %) was obtained as a white solid.

Phenol 30 mg (0.32 mmol) and potassium carbonate 44 mg (0.32 mmol) were added to acetonitrile

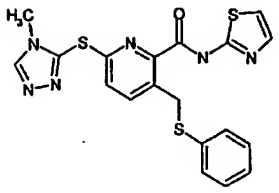
solution (5 ml) of 2-chloro-5-chloromethyl-6-cyanopyridine 50 mg (0.27 mmol), and thereafter the mixture was stirred at room temperature for eight hours 30 minutes. Water was added to the reaction liquid and the liquid extracted with ethyl acetate, and the organic layer was washed with saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using thin layer column chromatography (hexane : ethyl acetate = 6:1) and 2-chloro-6-cyano-5-phenoxymethyl pyridine 61 mg (yield = 93 %) was obtained as a white solid.

3-mercapto-4-methyl-4H-1,2,4-triazole 44 mg (0.380 mmol) and potassium carbonate 52 mg (0.380 mmol) were added to N,N-dimethylformamide solution (5 ml) of the obtained 2-chloro-6-cyano-5-phenoxymethyl pyridine 61 mg (0.249 mmol), and thereafter, it was stirred at 100°C overnight. Water was added to the reaction liquid and the liquid extracted with ethyl acetate, and the organic layer was washed with water, saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using thin layer column chromatography (chloroform : methanol = 10:1) and thio triazole derivative 4.4 mg (yield = 5 %) was obtained as a white solid.

A 1 N-sodium hydroxide aqueous solution 0.5 ml was added to ethanol solution (5 ml) of the obtained thio triazole derivative 4.4 mg (0.014 mmol) and the mixture was heated under reflux overnight. A 1 N hydrochloric acid aqueous solution was added to the reaction liquor, it was acidified, it was extracted with ethyl acetate, and the organic layer was washed with saturated aqueous sodium chloride solution. 2-aminothiazole 3 mg (0.028 mmol), N-hydroxybenzotriazole hydrate 4 mg (0.030 mmol) and 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride 6 mg (0.030 mmol) were added successively to the methylene chloride solution (3 ml) of obtained residue and thereafter, it was stirred at room temperature overnight. Saturated aqueous sodium bicarbonate solution was added to the reaction liquor, extraction was carried out with chloroform, and the organic layer was washed with water, saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was refined using thin layer silica gel chromatography (chloroform : methanol = 10:1) and the title compound 2.8 mg (yield = 47 %) was obtained as a white solid.
^{1}H-NMR ($CDCl_3$) d: 3.79 (3H, s), 5.71 (2H, s), 6.97-7.02 (3H, m), 7.05 (1H, d, J = 3.6 Hz), 7.30 (2H, t, J = 7.6 Hz), 7.40 (1H, d, J = 8.4 Hz), 7.54 (1H, q, J = 3.6 Hz), 8.22 (1H, d, J = 8.4 Hz), 8.50 (1H, s)
ESI-MS (m/e)= 425 (M+H).

Using the same process as in the aforesaid Production Example 69, the compound of Production Example 70 was obtained. Below analysis data of this compound are shown.

Production Example 70



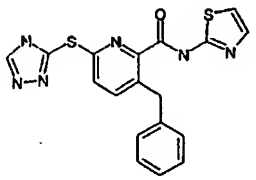
Preparation of 3-phenyl sulphanyl methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 70 can be produced using the same process as in Production Example 69, a process based on this or a combination of these with conventional procedures, using 2-cyano-3-tert-butyldimethylsilyloxy methylpyridine, thiophenol, 3-mercapto-4-methyl-4H-1,2,4-triazole and 2-aminothiazole.

^{1}H-NMR ($CDCl_3$) δ : 3.77 (3H, s), 4.74 (2H, s), 7.04 (1H, d, J = 3.2 Hz), 7.20 (1H, d, J = 8.4 Hz), 7.24-7.28 (5H, m), 7.53 (1H, d, J = 3.2 Hz), 7.58 (1H, d, J = 8.4 Hz), 8.48 (1H, s)

ESI-MS (m/e) = 441 (M+H).

Production Example 71



Preparation of 3-phenylmethyl-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

3-benzoyl-2-pyridinecarboxylic acid 2.0 g (8.8 mmol) was dissolved in methanol (10 ml), and ten drops of concentrated sulfuric acids were added dropwise at room temperature to this, and it was heated under reflux for twenty-four hours. After cooling, methanol was eliminated by distillation, and it was neutralized with saturated aqueous sodium bicarbonate solution. After extraction with chloroform, it was dried with sodium sulfate and concentrated, and thereby crude product 2.0 g of 3-benzoyl-2-methyl pyridinecarboxylate ester was obtained.

The ester body 2.0 g were dissolved in chloroform (10 ml), and mCPBA 3.57 g (20.7 mmol) was

added, and it was heated under reflux twenty-four hours. After cooling, saturated aqueous sodium bicarbonate solution was added to the reaction liquor, it was made alkaline, and extraction was carried out with chloroform. After drying with sodium sulfate, distillation was carried out under reduced pressure, and crude product of N-oxide was obtained. Phosphorus oxychloride (10 ml) was added to this crude product and was stirred at 80°C for two hours. After cooling, it was neutralized with saturated aqueous sodium bicarbonate solution and extraction was carried out with ethyl acetate. After drying with sodium sulfate and distillation under reduced pressure, the residue was refined by silica gel column chromatography (ethyl acetate : hexane = 1:2) and 3-benzoyl-6-chloro-2-methyl pyridinecarboxylate ester 600 mg (yield over 3 steps of 26 %) was obtained.

Chloro body 300 mg (1.10 mmol) was dissolved in methanol (15 ml), and 1 N sodium hydroxide (5 ml) was added, and the mixture was stirred at room temperature for two hours. After elimination of methanol by distillation, it was neutralized with 1 N hydrochloric acid, and thereafter, extraction was carried out with chloroform. After drying with sodlium sulphate, distillation was carried out under reduced pressure and thereby 285 mg (yield 100 %) of 3-benzoyl-6-chloro-2-pyridinecarboxylic acid was obtained.

The carboxylic acid 285 mg (1.1 mmol) obtained as above was dissolved in chloroform (10 ml), and 2-aminothiazole 109 mg (1.1 mmol), N-hydroxybenzotriazole hydrate 221 mg (1.64 mmol), 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride 229mg (1.2 mmol)-were added, and the mixture was stirred at room temperature twenty-four hours. Distilled water was added and thereafter, it was extracted with chloroform and drying was carried out with sodium sulfate. The solvent was eliminated by distillation under reduced pressure, the obtained residue was refined by column chromatography (ethyl acetate : hexane = 1:2) and 3-benzoyl-6-chloro-N-(thiazol-2-yl)-2-pyridinecarboxamide 225 mg (yield over 2 steps of 60 %) was obtained.

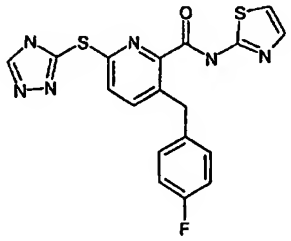
The chloro body 170 mg (0.495 mmol) obtained as above was dissolved in DMF (3 ml) and 3-mercapto-1,2,4-triazole 55 mg (0.544 mmol), potassium carbonate 171 mg (1.24 mmol) were added, and it was stirred at 100°C twenty-four hours. The reaction liquor was cooled, thereafter, DMF was eliminated by distillation under reduced pressure, distilled water was added, it was neutralized with 1 N hydrochloric acid, thereafter, distillation was carried out under reduced pressure, the obtained residue was refined by silica gel column chromatography (methanol : chloroform = 1:10) and 3-benzoyl-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide 101 mg (yield 50 %) was obtained.

The ketone body 70 mg (0.172 mmol) obtained as above was suspended in methanol (5 ml), sodium borohydride 12.7 mg (0.343 mmol) was added, the mixture was stirred at room temperature for 30 minutes, and the solvent was eliminated by distillation. Triethylsilane 99 mg (0.853 mmol) and trifluoroacetic acid (5 ml) were added to the obtained residue the mixture was stirried at 60 degrees for one hour. After concentrating, it was distributed with chloroform and saturated aqueous sodium bicarbonate solution, and the chloroform layer was dried with sodium sulfate. The solvent was concentrated, thereafter the obtained residue was refined twice using thin layer silica gel chromatography (methanol : chloroform = 1:8, ethyl acetate : acetone = 2:1) and the title compound 13.5 mg (yield 20 %) was obtained.

^{1}H-NMR ($CDCl_3$) d : 4.63 (2H, s), 6.99 (1H, d, J = 3.6 Hz), 7.18-7.29 (5H, m), 7.38 (1H, d, J = 8.4 Hz), 7.41 (1H, dd, J = 3.6 Hz), 7.45 (1H, d, J = 8.4 Hz), 8.33 (1H, s).

ESI-MS (m/e)= 395 $(M+H)^+$.

Production Example 72



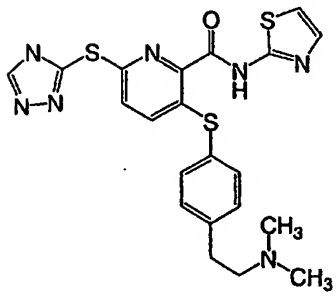
Preparation of 3-(4-fluoro-phenylmethyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

^{1}H-NMR ($CDCl_3$) δ : 4.60 (2H, s), 6.94-6.98 (2H, m), 7.01 (1H, d, J = 3.6 Hz), 7.14-7.17 (2H, m), 7.40-7.46 (3H, m), 8.35 (1H, s).

ESI-MS (m/e)= 413 $(M+H)^+$.

The compound of Production Example 72 can be produced using Production Example 71, a process based on this or a combination of these with conventional procedures, using 3-(4-fluorobenzoyl)-2-pyridinecarboxylic acid, 2-aminothiazole and 3-mercapto-1,2,4-triazole.

Production Example 73



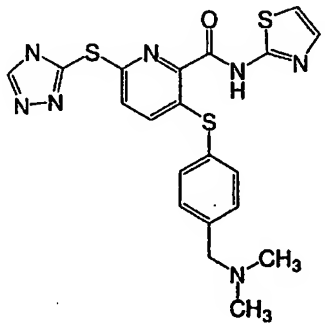
Preparation of 3-(4-dimethylaminoethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 73 can be produced using Production Example 71, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylaminoethyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.39 (6H, s), 2.68 (2H, m), 2.84(2H, m), 7.00-7.05 (2H, m), 7.18 (1H, d, J = 8.7 Hz), 7.28 (2H, q, J = 8.4 Hz), 7.41-7.58 (3H, m), 8.32 (1H, s).

ESI-MS (m/e) = 484 $(M+H)^+$.

Production Example 74



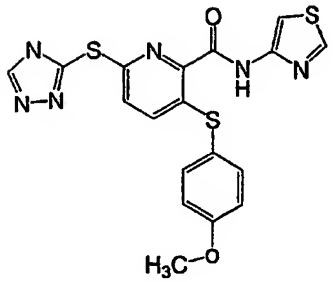
Preparation of 3-(4-dimethylaminomethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 74 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylaminomethyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.23 (6H, s), 6.96 (1H, q, J = 8.8 Hz), 7.00 (1H, d, J = 3.6 Hz), 7.11 (1H, d, J =

3.8 Hz), 7.34 (2H, d, J = 8.0 Hz), 7.43 (1H, d, J = 3.6 Hz), 7.46 (2H, d, J = 8.0 Hz), 8.29 (1H, s).
ESI-MS (m/e) = 470 $(M+H)^+$.

Production Example 75

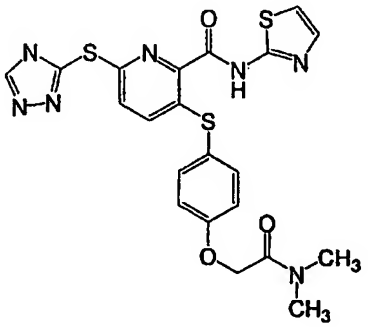


Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-4-yl)-2-pyridinecarboxamide

The compound of Production Example 75 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 4-amino-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.85 (3H, s), 6.96 (2H, d, J = 8.8 Hz), 6.98 (1H, d, J = 8.8 Hz), 7.15 (1H, d, J = 8.8 Hz), 7.46 (2H, d, J = 8.3 Hz), 7.90 (1H, d, J = 2.4 Hz), 8.34 (1H, s), 8.61 (1H, d, J = 2.4 Hz),
ESI-MS (m/e)= 443 $(M+H)^+$.

Production Example 76



Preparation of 3-(4-dimethylcarbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

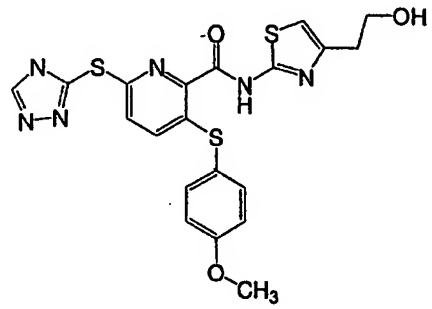
The compound of Production Example 76 can be produced using the same process as in Production

Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylcarbamoylmethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.99 (3H, s), 3.09 (3H, s), 4.73 (2H, s), 6.99 (2H, d, J = 3.8 Hz), 7.01-7.03 (1H, m), 7.03 (1H, d, J = 3.6 Hz), 7.19 (2H, d, J = 8.4 Hz), 7.45 (2H, d, J = 8.8 Hz), 7.46 (2H, d, J = 3-6 Hz), 8.30 (1H, s).

ESI-MS (m/e) 514 $(M+H)^+$.

Production Example 77



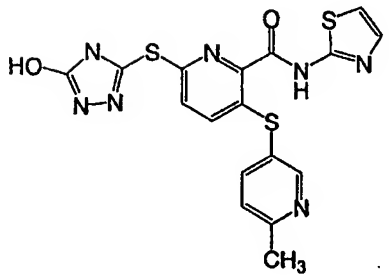
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(4-hydroxyethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 77 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-hydroxyethyl-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.90 (2H, t, J = 4.8 Hz), 3.83 (3H, s), 3.90 (2H, t, J = 4.8 Hz), 6.65 (1H, s), 6.95 (2H, d, J = 8.0 Hz), 6.97 (1H, d, J = 8.8 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.43 (2H, d, J = 8.0 Hz), 8.34 (1H, s).

ESI-MS (m/e) = 487 $(M+H)^+$.

Production Example 78



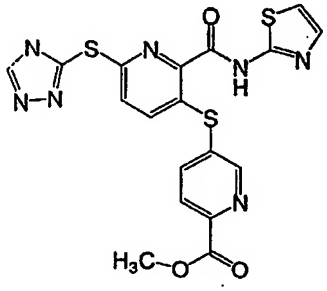
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 78 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-hydroxy-thiophenol and 5-hydroxy-3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.65 (3H, s), 6.98-7.50 (5H, m), 7.82 (1H, m), 8.64 (1H, brs),

ESI-MS (m/e) = 444 $(M+H)^+$.

Production Example 79



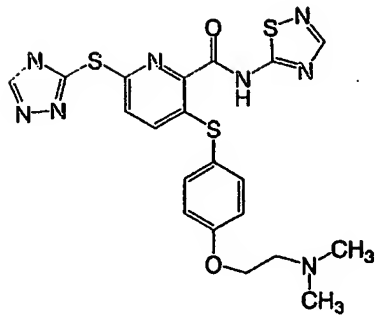
Preparation of 3-(6-methoxycarbonyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 79 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained using the same process as in Production Example 1, 5-iodo-2-methoxycarbonyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 4.01 (3H, s), 7.03 (1H, d, J = 7.6 Hz), 7.05 (1H, d, J = 3.6 Hz), 7.24 (1H, d, J = 7.6 Hz), 7.47 (1H, d, J = 3.6 Hz), 8.00 (1H, m), 8.16 (1H, d, J = 8.0 Hz), 8.33 (1H, s), 8.79 (1H, m).

ESI-MS (m/e) = 472 $(M+H)^+$.

Production Example 80



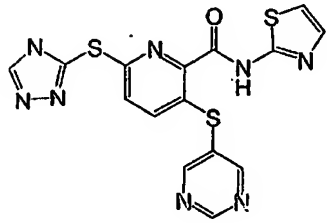
Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 80 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-1,2,4-thiadiazole, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.42 (6H, s), 2.84 (2H, t, J = 5.1 Hz), 4.13 (2H, t, J = 5.1 Hz), 6.96 (2H, d, J = 8.4 Hz), 7.00 (1H, d, J = 8.8 Hz), 7.21 (1H, d, J = 8.8 Hz), 7.43 (2H, d, J = 8.4 Hz), 8.35 (1H, s).

ESI-MS (m/e) = 501 $(M+H)^+$.

Production Example 81

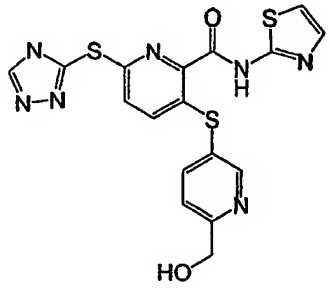


Preparation of 3-(pyrimidin-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 81 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained using the same method as in Production Example 1, 5-iodo-pyrimidine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.95 (1H, d, J = 8.4 Hz), 7.03 (1H, d, J = 3.6 Hz), 7.22 (1H, d, J = 8.4 Hz), 7.44 (1H, d, J = 3.6 Hz), 8.33 (1H, s), 8.82 (2H, s), 9.20 (1H, s).
ESI-MS (m/e) = 415 $(M+H)^+$.

Production Example 82

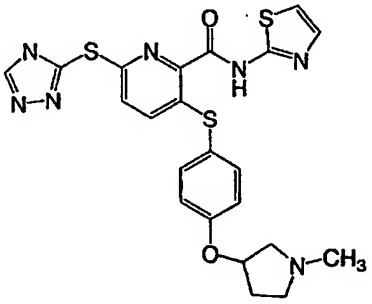


Preparation of 3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 32 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-hydroxymethyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 4.86 (2H, s), 7.01 (1H, d, J = 9.2 Hz), 7.07 (1H, d, J = 3.2 Hz), 7.28 (1H, d, J = 9.2 Hz), 7.41 (1H, d, J = 7.6 Hz), 7.52 (1H, d, J = 3.2 Hz), 7.90 (1H, m), 8.42 (1H, s), 8.74 (1H, s).
ESI-MS (m/e) = 444 $(M+H)^+$.

Production Example 83



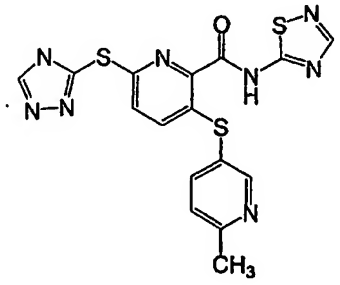
Preparation of 3-[4-(1-methyl-pyrrolidine-3-yloxy)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 83 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-(1-methyl-pyrrolidin-3-yl)-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.90-1.98 (1H, m), 2.35 (3H, s), 2.25-2.35 (2H, m), 2.43-2.47 (1H, m), 2.80-2.83 (2H, m), 4.78-4.85 (1H, m), 6.85 (2H, d, J = 8.4 Hz), 6.95 (1H, d, J = 8.8 Hz), 7.00 (1H, d, J = 3.6 Hz), 7.12 (1H, d, J = 8.8 Hz), 7.38 (2H, d, J = 8.4 Hz), 7.42 (1H, d, J = 3.6 Hz), 8.29 (1H, s).

ESI-MS (m/e) = 512 $(M+H)^+$.

Production Example 84



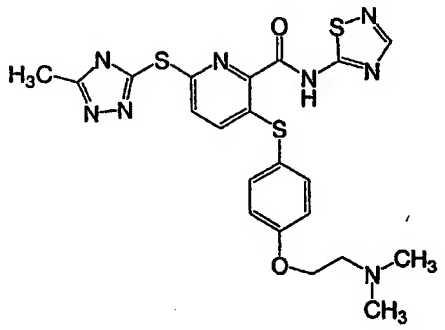
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 84 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-1,2,4-thiadiazole-3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.65 (3H, s), 7.01 (1H, d, J = 8.6 Hz), 7.26 (1H, d, J = 8.6 Hz), 7.30 (1H, d, J = 8.0 Hz), 7.78 (1H, dd, J = 8.0, 2.2 Hz), 8.35 (1H, s), 8.42 (1H, s), 8.64 (1H, d, J = 2.2 Hz).

ESI-MS (m/e) = 429 $(M+H)^+$.

Production Example 85



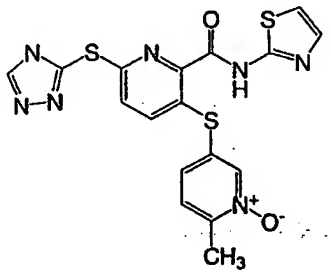
Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 85 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-1,2,4-thiadiazole, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.40 (6H, s), 2.62 (6H, s), 2.81 (2H, t, J = 5.5 Hz), 4.12 (2H, t, J = 5.1 Hz), 6.96 (2H, d, J = 8.5 Hz), 6.98 (1H, d, J = 8.5 Hz), 7.20 (1H, d, J = 8.5 Hz), 7.42 (2H, d, J = 8.5 Hz), 8.34 (1H, s).

ESI-MS (m/e) = 515 $[M+H]^+$.

Production Example 86

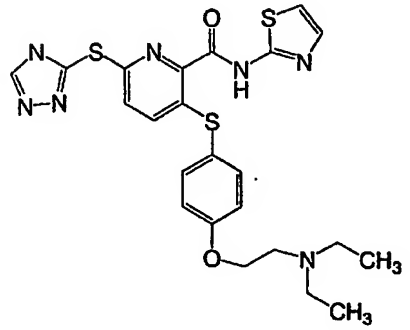


Preparation of 3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 86 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-mercapto-6H methyl-1-oxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.60 (3H, s), 7.06 (1H, d, J = 3.2 Hz), 7.12 (1H, d, J = 8.4 Hz), 7.32 (1H, q, J = 8.4 Hz), 7.39-7.39 (2H, m), 7.51 (1H, d, J = 3.2 Hz), 8.44 (1H, s), 8.51 (1H, brs).
ESI-MS (m/e) = 446 (M+H).

Production Example 87

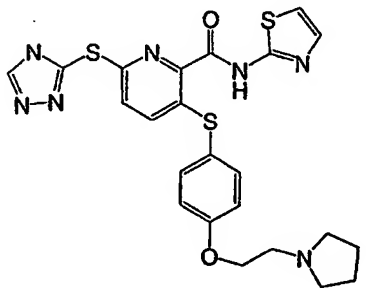


Preparation of 3-(4-diethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 87 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-diethylaminoethyl oxy-thiophenol and 3-mercapto-1, 2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.14 (6H, t, J = 7.6 Hz), 2.73 (4H, q, J = 7.6 Hz), 2.99 (2H, t, J = 6.0 Hz), 4.14 (2H, t, J = 6.0 Hz), 6.99 (2H, q, J = 8.8 Hz), 7.01 (1H, d, J = 8.4 Hz), 7.07 (1H, d, J = 4.0 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.49 (1H, d, J = 4.0 Hz), 8.36 (1H, s).
ESI-MS (m/e) = 528 $(M+H)^+$.

Production Example 88



Preparation of 3-(4-pyrrolidino ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-

(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 88 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-pyrrolidino ethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.80-1.90 (4H, m), 2.70-2.80 (4H, m), 3.02 (2H, t, J = 5.2 Hz), 4.18 (2H, t, J = 5.2 Hz), 6.95 (2H, q, J = 3.8 Hz), 6.97 (1H, d, J = 8.4 Hz), 7.02 (1H, q, J = 3.6 Hz), 7.17 (1H, d, J = 8.4 Hz), 7.42 (2H, d, J = 8.8 Hz), 7.45 (1H, d, J = 3.6 Hz), 8.29 (1H, s).

ESI-MS (m/e) = 526 $(M+H)^+$.

Production Example 89

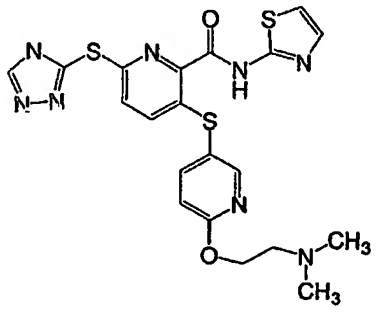
Preparation of 3-(4-diethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 87 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-diethylaminoethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.14 (6H, t, J = 7.6 Hz), 2.73 (4H, q, J = 7.6 Hz), 2.99 (2H, t, J = 6.0 Hz), 4.14 (2H, t, J = 6.0 Hz), 6.99 (2H, d, J = 8.8 Hz), 7.01 (1H, d, J = 8.4 Hz), 7.07 (1H, d, J = 4.0 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.46 (2H, d, J = 8.8 Hz), 7.49 (1H, d, J = 4.0 Hz), 8.36 (1H, s)

ESI-MS(m/e) = 528 $(M+H)^+$.

Production Example 88 (sic)



Preparation of 3-(6-dimethylaminoethyl oxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

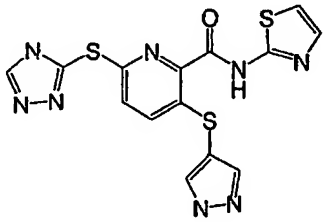
The compound of Production Example 89 can be produced using the same process as in Production

Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-mercapto-6-dimethylaminoethyl oxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.41 (6H, s), 2.82 (2H, t, J = 5.6 Hz), 4.48 (2H, t, J = 5.6 Hz), 6.80 (1H, d, J = 8.4 Hz), 6.98 (1H, d, J = 8.4 Hz), 7.03 (1H, d, J = 3.6 Hz), 7.23 (1H, d, J = 8.4 Hz), 7.47 (1H, d, J = 3.6 Hz), 7.63 (1H, dd, J = 2.4, 8.4 Hz), 7.27 (1H, d, J = 2.4 Hz), 8.36 (1H, s).

ESI-MS (m/e) = 501 $(M+H)^+$.

Production Example 90



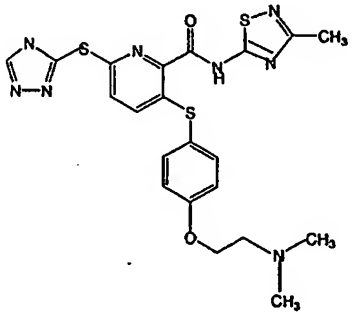
Preparation of 3-(pyrazol-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 90 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained using the same method as in Production Example 1, 4-iodo pyrazole and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 7.07 (1H, d, J = 3.6 Hz), 7.18 (1H, d, J = 8.4 Hz), 7.25 (1H, d, J = 8.4 Hz), 7.49 (1H, d, J = 3.6 Hz), 7.70 (2H, s), 8.35(1H, s).

ESI-MS (m/e) = 403 $(M+H)^+$.

Production Example 91



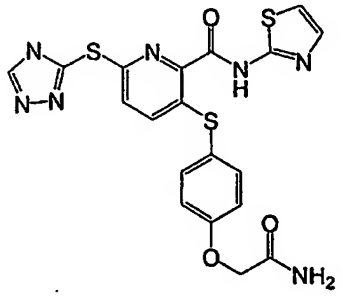
Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 91 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.37 (6H, s), 2.61 (3H, s), 2.80 (2H, t, J = 5.6 Hz), 4.12 (2H, t, J = 5.6 Hz), 7.00 (2H, d, J = 8.4 Hz), 7.02 (1H, d, J = 8.8 Hz), 7.22 (1H, d, J = 8.8 Hz), 7.45 (2H, d, J = 8.4 Hz), 8.34 (1H, s).

ESI-MS (m/e) = 515 $(M+H)^+$.

Production Example 92



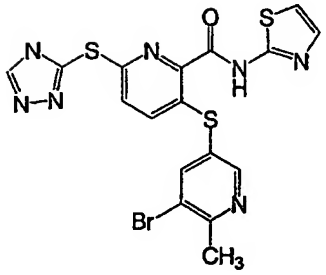
Preparation of 3-(4-carbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 92 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-carbamoylmethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 4.48 (2H, s), 6.95 (1H, d, J = 8.4 Hz), 6.98 (2H, d, J = 8.8 Hz), 7.02 (1H, d, J = 3.6 Hz), 7.13 (1H, d, J = 8.4 Hz), 7.44 (1H, d, J = 3.6 Hz), 7.45 (2H, d, J = 8.8 Hz), 8.33 (1H, s).

ESI-MS (m/e) = 486 $(M+H)^+$.

Production Example 93



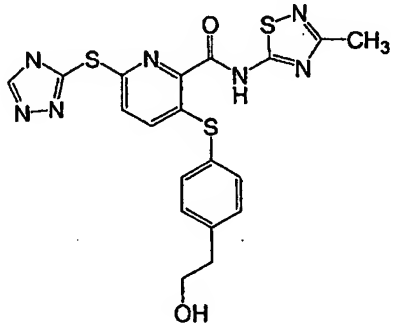
Preparation of 3-(5-bromo-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 93 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 5-bromo-3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.72 (3H, s), 7.00 (1H, d, J = 8.4 Hz), 7.05 (1H, d, J = 3.6 Hz), 7.22-7.24 (1H, m), 7.48 (1H, q, J = 8.6 Hz), 8.01 (1H, d, J = 2.0 Hz), 8.33 (1H, s), 8.52 (1H, d, J = 2.0 Hz).

ESI-MS (m/e) = 505, 507 $(M+H)^+$.

Production Example 94



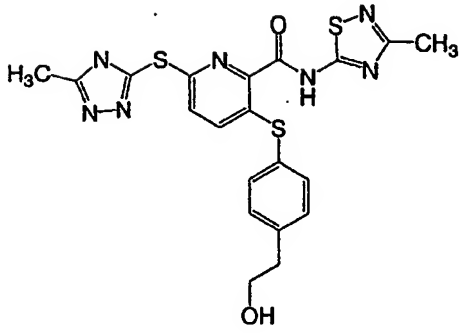
Preparation of 3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 94 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-(2-hydroxyethyl)-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.61 (3H, s), 2.91 (2H, t, J = 6.8 Hz), 3.84 (2H, t, J = 6.8 Hz), 7.07 (1H, d, J = 8.4 Hz), 7.21 (1H, d, J = 8.4 Hz), 7.35 (2H, d, J = 8.0 Hz), 7.48 (2H, d, J = 8.0 Hz), 8.36 (1H, s).

ESI-MS (m/e) = 472 $(M+H)^+$.

Production Example 95



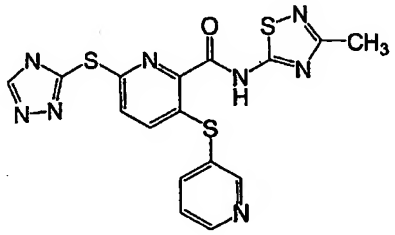
Preparation of 3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 95 is produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole-4-(2-hydroxyethyl)-thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.59 (3H, s), 2.59 (3H, s), 2.94 (2H, t, J = 6.4 Hz), 3.94 (2H, t, J = 6.4 Hz), 7.03 (1H, d, J = 8.8 Hz), 7.21 (1H, d, J = 8.8 Hz), 7.34 (2H, d, J = 8.0 Hz), 7.49 (2H, d, J = 8.0 Hz).

ESI-MS (m/e)= 486 $(M+H)^+$.

Production Example 96



Preparation of 3-(pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

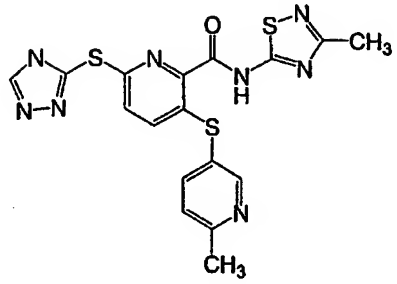
The compound of Production Example 96 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-pyridine and 3-

mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.61 (3H, s), 7.00 (1H, d, J = 8.8 Hz), 7.29 (1H, d, J = 8.8 Hz), 7.41-7.44 (1H, m), 7.88-7.91 (1H, m), 8.41 (1H, s), 8.71-8.73 (1H, m), 8.76-8.77 (1H, m).

ESI-MS (m/e) = 429 $(M+H)^+$.

Production Example 97



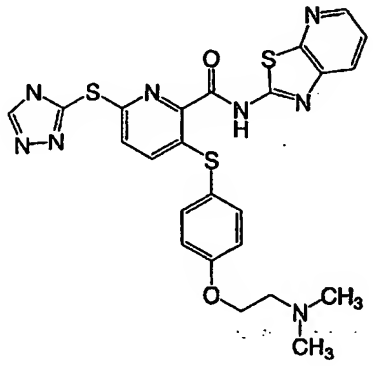
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 97 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.62 (3H, s), 2.64 (3H, s), 7.2 (1H, q, J = 8.0 Hz), 8.35 (1H, s), 8,60 (1H, d, J = 1.6 Hz).

ESI-MS (m/e) = 443 $(M+H)^+$.

Production Example 98



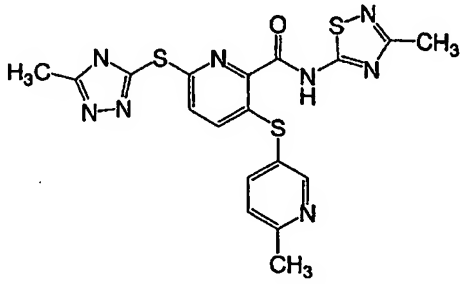
Preparation of 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [5,4-b] pyridin-2-yl)-2-pyridinecarboxamide

The compound of Production Example 98 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazolo [5,4-b] pyridine, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.43 (6H, s), 2.70-2.88 (2H, m), 4.08-4.14 (2H, m), 6.88 (2H, d, J = 8.4 Hz), 6.89-6.93 (1H, m), 7.13 (1H, d, J = 8.8 Hz), 7.31-7.35 (1H, m), 7.38 (2H, d, J = 8.8 Hz), 7,96 (1H, d, J = 8.4 Hz), 8.37 (1H, s), 8.44 (1H, d, J = 4.0 Hz).

ESI-MS (m/e) = 551 $(M+H)^+$.

Production Example 99



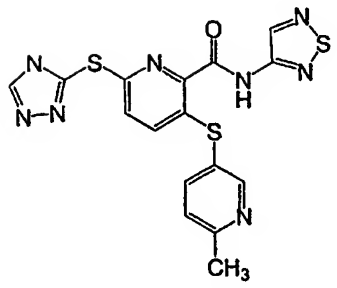
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 99 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2H pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) d : 2.60 (3H, s), 2.61 (3H, s), 3.64 (3H, s), 7.0 (1H, q, J = 8.8 Hz), 7.20-7.36 (1H, m), 7.29 (1H, d, J = 8.0 Hz), 7.77 (1H, dd, J = 2.4, 8.0 Hz), 8.63 (1H, d, J = 2.4 Hz).

ESI-MS (m/e) = 457 $(M+H)^+$.

Production Example 100



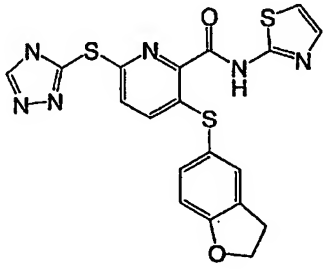
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,5] thiadiazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 100 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1,2,5-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.63 (3H, s), 6.99 (1H, d, J = 8.8 Hz), 7.21 (1H, d, J = 8.8 Hz), 7.29 (1H, q, J = 8.1 Hz), 7.78 (1H, dd, J= 8.1, 2.2 Hz), 8.37 (1H, s), 8.60 (1H, d, J = 2.2 Hz), 9.38 (1H, s).

ESI-MS (m/e) = 429 $(M+H)^+$.

Production Example 101



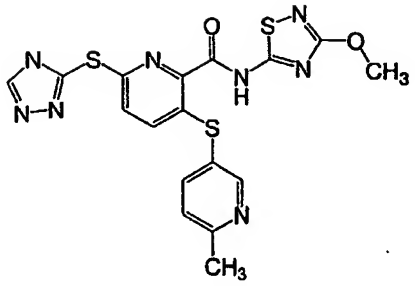
Preparation of 3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 101 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained by the same method as in Production Example 1, 5-iodo-2,3-dihydro-benzofuran and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.26 (2H, t, J = 8.8 Hz), 4.66 (2H, t, J= 8.8 Hz), 6.86 (1H, q, J = 8.0 Hz), 7.02 (1H, d, J = 3.2 Hz), 7.06 (1H, d, J = 8.8 Hz), 7.22 (1H, d, J = 8.8 Hz), 7.31 (1H, d, J = 8.0 Hz), 7.35

(1H, brs), 7.45 (1H, d, J = 3.2 Hz), 8.34 (1H, s).
ESI-MS (m/e) = 455 $(M+H)^+$.

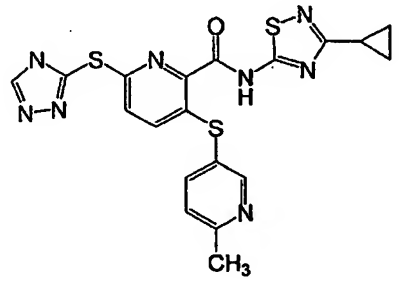
Production Example 102



Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methoxy-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 102 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methoxy-1,2,4-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 2.65 (3H, s), 4.08 (3H, s), 6.90-7.05 (1H, m), 7.10-7.30 (2H, m), 7.70-7.80 (1H, m), 8.39 (1H, s), 8.63 (1H, brs).
ESI-MS (m/e) = 459 $(M+H)^+$.

Production Example 103



Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-cyclopropyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

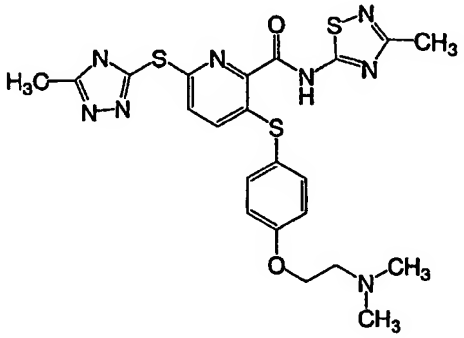
The compound of Production Example 103 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-

dichloro-2-pyridinecarboxylic acid, 5-amino-3-cyclopropyl-1,2,4-thiadiazole-3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 0.90-1.20 (4H, m), 2.20-2.35 (1H, m), 2.64 (3H, s), 6.99 (1H, q, J = 8.8 Hz), 7.20-7.30 (2H, m), 7.76 (1H, dd, J = 2.4, 8.0 Hz), 8.38 (1H, s), 8.62 (1H, brs).

ESI-MS (m/e) = 469 $(M+H)^+$.

Production Example 104



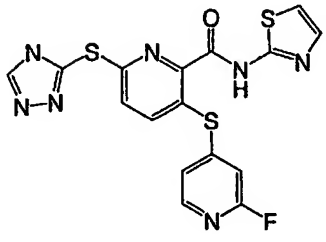
Preparation of 3-(4-distill amino ethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41 thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 104 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-dimethylaminoethyl oxy-thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.41 (6H, s), 2.58 (3H, s), 2.59 (3H, s), 2.83 (2H, t, J = 5.5 Hz), 4.12 (2H, t, J = 5.5 Hz), 6.91 (2H, d, J = 8.8 Hz), 6.94 (1H, d, J = 8.6 Hz), 7.17 (1H, d, J = 8.6 Hz), 7.40 (2H, d, J = 8.8 Hz).

ESI-MS (m/e) = 529 $(M+H)^+$.

Production Example 105



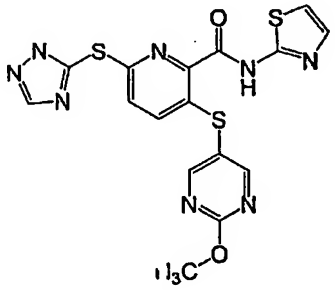
Preparation of 3-(2-fluoro-pyridin-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 105 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained by the same method as in Production Example 1, 2-fluoro-4-iodo-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.95-7.10 (2H, m), 7.20-7.26 (2H, m), 7.30-7.42 (1H, m), 7.40-7.50 (1H, m), 8110-8.26 (1H, m), 8.38-8.45 (1H, m).

ESI-MS (m/e) = 432 $(M+H)^+$.

Production Example 106



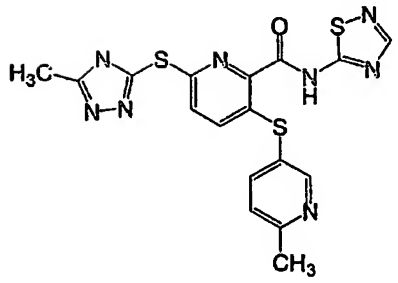
Preparation of 3-(2-methoxy-pyrimidin-5-yl sulphanyl)-6-(2H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 106 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide obtained using the same method as in Production Example 1, 5-iodo-2-methoxy-pyrimidine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 4.10 (3H, s), 7.02 (1H, d, J = 8.4 Hz), 7.06 (1H, d, J = 3.6 Hz), 7.32 (1H, d, J = 8.4 Hz), 7.50 (1H, d, J = 3.6 Hz), 8.39 (1H, s), 8.65 (2H, s).

ESI-MS (m/e) = 445 $(M+H)^+$.

Production Example 107



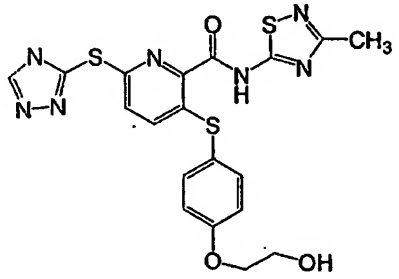
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 107 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-1,2,4-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.62 (3H, s), 2.64 (3H, s), 6.99 (1H, d, J = 8.8 Hz), 7.20-7.35 (2H, m), 7.77 (1H, dd, J = 2.0, 8.0 Hz), 8.35 (1H, s), 8.63 (1H, brs).

ESI-MS (m/e) 443 $(M+H)^+$.

Production Example 108



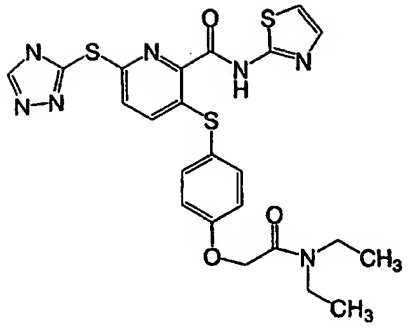
Preparation of 3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 108 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-hydroxyethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.63 (3H, s), 3.99 (2H, m), 4.13 (2H, m), 7.00-7.08 (3H, m), 7.25 (1H, d, J = 8.4 Hz), 7.49 (2H, d, J = 8.7 Hz), 8.36 (1H, s).

ESI-MS (m/e) = 488 $(M+H)^+$.

Production Example 109



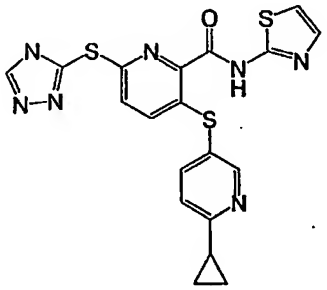
Preparation of 3-(4-diethylcarbamoyl methyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 109 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-diethylcarbamoylmethyloxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.72 (6H, s), 7.02 (1H, d, J = 3.6 Hz), 7.03 (1H, d, J = 8.0 Hz), 7.20 (1H, d, J = 8.0 Hz), 7.44 (1H, d, J = 3.6 Hz), 7.66 (2H, d, J = 8.4 Hz), 7.78 (2H, d, J = 8.4 Hz), 8.31 (1H, s).

ESI-MS (m/e) = 542 $(M+H)^+$.

Production Example 110



Preparation of 3-(6-cyclopropyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

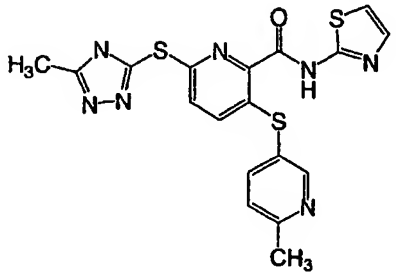
The compound of Production Example 110 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 6-cyclopropyl-3-mercapto-pyridine and 3-

mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 0.70-1.33 (4H, m), 1.98-2.18 (1H, m), 6.96-7.08 (2H, m), 7.46 (1H, d, J = 3.2 Hz), 7.70 (1H, dd, J = 2.0, 8.4 Hz), 8.36 (1H, s), 8.56 (1H, d, J = 2.0 Hz).

ESI-MS (m/e) = 453 $(M+H)^+$.

Production Example 111



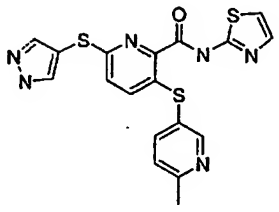
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 111 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.57 (3H, s), 2.64 (3H, s), 6.96 (1H, d, J = 8.8 Hz), 7.02 (1H, d, J = 3.6 Hz), 7.20 (1H, q, J = 8.8 Hz), 7.25-7.29 (1H, m), 7.46 (1H, d, J = 3.6 Hz), 7.76 (1H, dd, J = 2.4, 7.6 Hz), 8.63 (1H, s).

ESI-MS (m/e)= 442 $(M+H)^+$.

Production Example 112



Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(pyrazol-4-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide

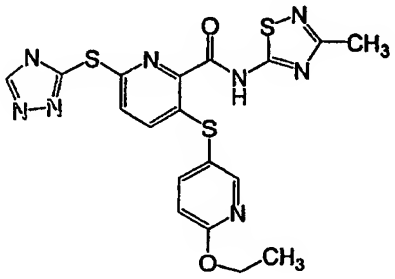
The compound of Production Example 112 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-

dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-mercapto-6-methyl-pyridine and 4-mercapto-pyrazole.

^{1}H-NMR ($CDCl_3$) δ : 2,62 (3H, s), 6.88(1H, m), 7.05 (1H, m), 7.24 (1H, d, J = 8.9 Hz), 7.30-7.68 (3H, m), 7.72 (1H, dd, J = 1.1, 8.9 Hz), 7.76-7.82 (1H, m), 8.60 (1H, d, J = 1.1 Hz)

ESI-MS (m/e) = 427 $(M+H)^+$.

Production Example 113



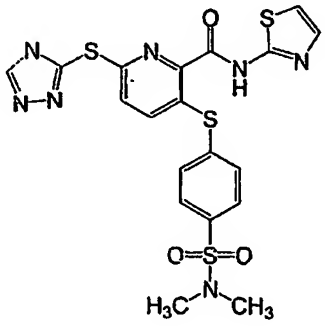
Preparation of 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 113 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-hydroxy-1,2,4-thiadiazole, 6-ethoxy-3-mercapto-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.43 (3H, t, J = 6.9 Hz), 2.06 (3H, s), 4.42 (2H, q, J = 6.9 Hz), 6.85 (1H, d, J = 9.0 Hz), 7.08 (1H, d, J = 9.0 Hz), 7.29 (1H, d, J = 9.0 Hz), 7.69 (1H, dd, J = 9.0, 2.1 Hz), 8.31 (1H, d, J = 2.1 Hz), 8.37 (1H, s).

ESI-MS (m/e) = 473 $(M+H)^+$.

Production Example 114



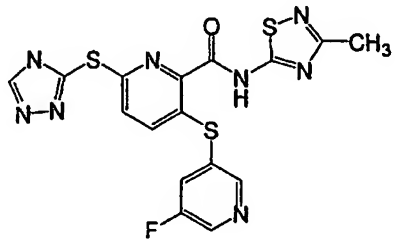
Preparation of 3-(4-dimethylamino sulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 114 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-dimethylaminosulfonyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.72 (6H, s), 7.02 (1H, d, J = 3.6 Hz), 7.03 (1H, d, J = 8.0 Hz), 7.20 (1H, d, J = 8.0 Hz), 7.44 (1H, d, J = 3.6 Hz), 7.66 (2H, d, J = 8.4 Hz), 7.78 (2H, d, J = 8.4 Hz), 8.33 (1H, s).

ESI-MS (m/e) = 520 $(M+H)^+$.

Production Example 115



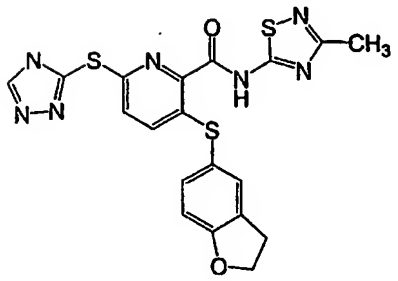
Preparation of 3-(5-fluoro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 115 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 5-fluoro-3-mercapto-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.59 (3H, s), 7.02 (1H, d, J = 8.8 Hz), 7.30 (1H, d, J = 8.4 Hz), 7.60-7.75 (1H, m), 8.41 (1H, s), 8.50-8.65 (2H, m).

ESI-MS (m/e) = 447 $(M+H)^+$.

Production Example 116



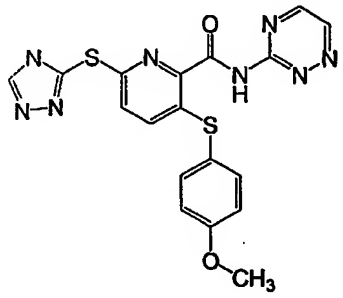
Preparation of 3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 116 can be produced by the process sentence which followed-this the same method as in Production Example 66 using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridinecarboxamide obtained using the same method as in Production Example 1, 5-iodo-2,3-dihydro-benzofuran and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.61 (3H, s), 3.25 (2H, t, J = 8.4 Hz), 4.65 (2H, t, J = 8.4 Hz), 6.85 (1H, d, J = 8.4 Hz), 7.05 (1H, d, J = 8.4 Hz), 7.06-7.33 (3H, m), 7.78 (1H, dd, J = 2.4, 8.5 Hz), 8.31 (1H, s).

ESI-MS (m/e) = 470 $(M+H)^+$.

Production Example 117



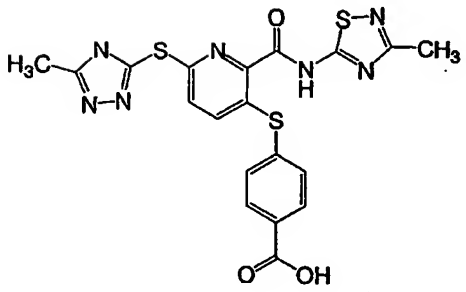
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4]-triazine-3-yl)-2-pyridinecarboxamide

The compound of Production Example 117 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1,2,4-triazine, 4-methoxy-thiophenol and 3-amino-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.84 (3H, s), 6.95 (2H, q)J= 8.3 Hz), 7.0 (1H, d, J = 3-8 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.44 (2H, q, J = 8.8 Hz), 8.40 (1H, s), 8.63 (1H, d, J = 2.4 Hz), 8.96 (1H, d, J = 2.4 Hz).

ESI-MS (m/e) = 439 $(M+H)^+$.

Production Example 118



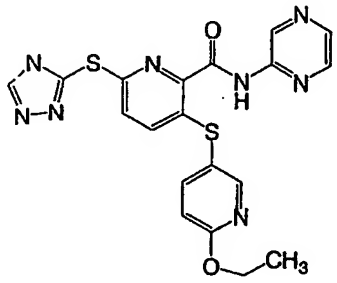
Preparation of 3-(4-carboxy-phenyl sulphanyl)-6-(5-methyl-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 118 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-carboxy-thiophenol and 3-mercapto-5-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.46 (3H, s), 2.52 (3H, s), 7.00 (1H, q, J = 8.8 Hz), 7.13 (1H, q, J = 8.8 Hz), 7.52 (2H, d, J = 7.8 Hz), 8.01 (2H, d, J = 8.0 Hz).

ESI-MS (m/e)= 486 $(M+H)^+$.

Production Example 119



Preparation of 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide

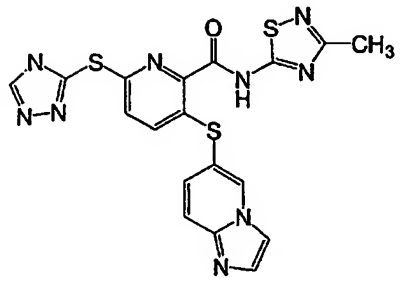
The compound of Production Example 119 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-pyrazine, 6-ethoxy-3-mercapto-pyridine and 3-mercapto-

1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.43 (3H, t, J = 6.9 Hz), 4.41 (2H, q, J = 6.9 Hz), 6.83 (1H, d, J = 8.7 Hz), 7.06 (1H, d, J = 8.7 Hz), 7.27 (1H, q, J = 8.7 Hz), 7.69 (1H, m), 8.29-8.35 (2H, m), 8.40 (1H, m), 8.42 (1H, s), 9.75 (1H, m).

ESI/MS(m/e) = 453 $(M+H)^+$.

Production Example 120



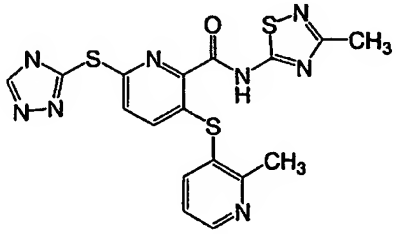
Preparation of 3-(imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 120 can be produced using the same process as in Production Example 66, a process based on this or a combination of these with conventional procedures, using 6-chloro-3-(4-methoxy-phenylmethyl sulphanyl)-N-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridine carboxamide obtained using the same process as in Production Example 1, 6-iodo-imidazo-[1,2-a]-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR (DMSO-d_6) δ = 3.30 (3H, s), 7.10-7.40 (3H, m), 7.60-7.80 (2H, m), 7.97 (1H, s), 8.60-8.80 (1H, m), 8.93 (1H, s).

ESI-MS (m/e) = 468 $(M+H)^+$.

Production Example 121



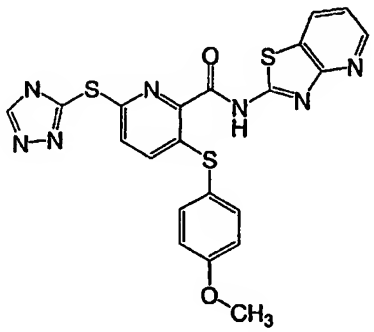
Preparation of 3-(2-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 121 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-2-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.59 (3H, s), 2.62 (3H, s), 6.84 (1H, d, J = 8.8 Hz), 7.20-7.35 (2H, m), 7.80-7.92 (1H, m), 8.43 (1H, s), 8.60-8.68 (1H, s).

ESI-MS (m/e)= 443 $(M+H)^+$.

Production Example 122



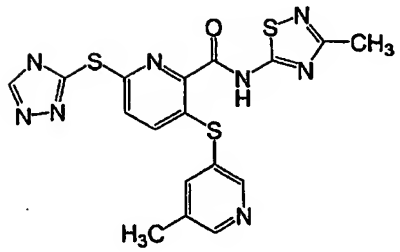
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [4,5-b] pyridine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 122 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazolo [4,5-b] pyridine, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.88 (3H, s), 7.01 (2H, q, J = 8.3 Hz), 7.03 (1H, d, J = 8.0 Hz), 7.02-7.26 (1H, m), 7.50 (2H, d, J = 8.8 Hz), 8.23 (1H, d, J = 8.0 Hz), 8.52 (1H, s), 8.59 (1H, s).

ESI-MS (m/e) = 494 $(M+H)^+$.

Production Example 123



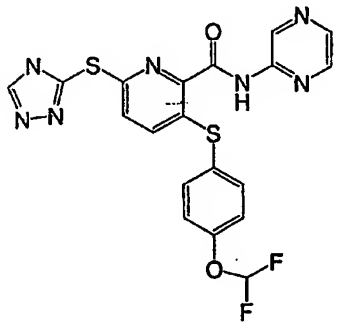
Preparation of 3-(5-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 123 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-5-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.40 (3H, s), 2.60 (3H, 3), 6.99 (1H, d, J= 8.4 Hz), 7.22-7.30(1H, m), 7.71 (1H, s), 8.40 (1H, s), 8.55 (2H, m).

ESI-MS (m/e) = 443 $(M+H)^+$.

Production Example 124



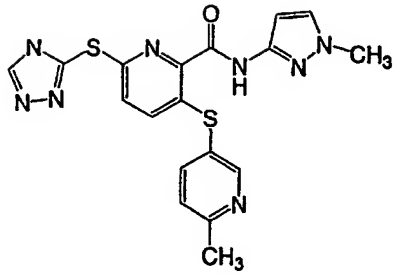
Preparation of 3-(4,4-difluoromethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 124 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-pyrazine, 4,4-difluoromethyl oxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.62 (1H, t, J = 73 Hz), 7.05 (1H, d, J = 9.0 Hz), 7.20-7.30(3H, m), 7.60 (2H, d, J = 8.7 Hz), 8.30-8.43 (2H, m), 8.41 (1H, brs), 9.78 (1H, brs).

ESI-MS (m/e) = 474 (M+H) +.

Production Example 125



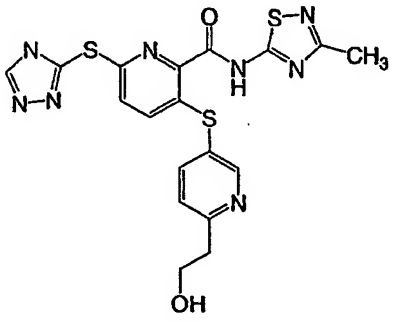
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 125 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.64 (3H, s), 3.89(3H, s), 6.91(1H, m) 6.97 (1H, d, J = 8.4 Hz), 7.17-7.36 (3H, m), 7.79(1H, m), 8.31 (1H, s), 8.63 (1H, m).

ESI-MS (m/e) = 425 $(M+H)^+$.

Production Example 126



Preparation of 3-(6-hydroxyethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]In thiadiazol-5-yl)-2-pyridinecarboxamide

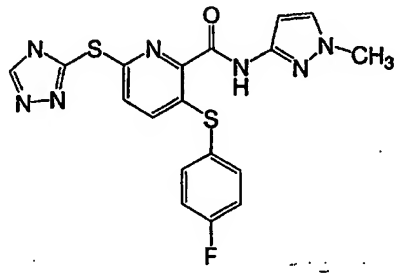
The compound of Production Example 126 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 6-hydroxyethyl-3-mercapto-

pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.57 (3H, s), 3.04 (2H, t, J = 6.0H), 3.97 (2H, t, J = 6.0 Hz), 6.98 (1H, d, J = 8.8 Hz), 7.20 (1H, d, J = 8.8 Hz), 7.30 (1H, d, J = 8.0 Hz), 7.78 (1H, dd, J = 2.4, 8.0 Hz), 8.32 (1H, s), 8.57 (1H, d, J = 2.4 Hz).

ESI-MS (m/e) = 473 $(M+H)^+$.

Production Example 127



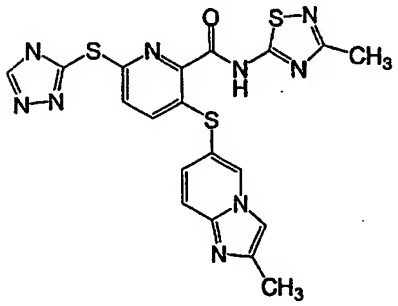
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 127 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-mercapto-1-methyl-1H-[1,2] pyrazole, 4-fluoro-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.85 (3H, s), 6.89 (1H, brs), 6.97 (1H, q, J = 8.7 Hz), 7.11-7.21 (3H, m), 7.30 (1H, d, J = 8.7 Hz), 7.57 (2H, m), 8.35 (1H, s).

ESI-MS (m/e) = 428 $(M+H)^+$.

Production Example 128



Preparation of 3-(2-methyl-imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl

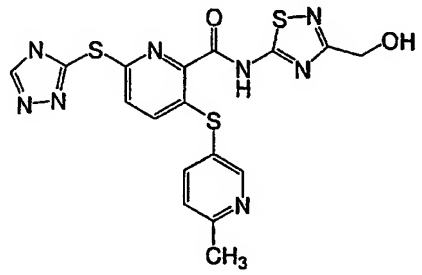
sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 128 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 6-mercapto-2-methyl-imidazo-[1,2-a] pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR (DMSO-d_6) δ : 2.34 (3H, s), 2.50 (3H, s), 7.10-7.20 (2H, m), 7.28 (1H, d, J = 8.4 Hz), 7.49 (1H, d, J = 9.2 Hz), 7.70 (1H, s), 8.70 (1H, brs), 8.83 (1H, s).

ESI-MS (m/e) = 482 $(M+H)^+$.

Production Example 129



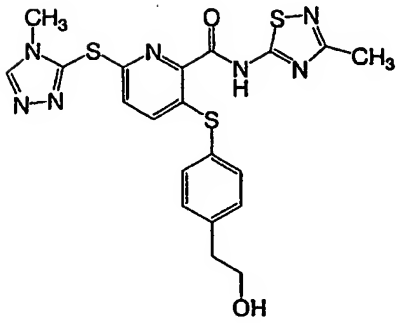
Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-hydroxymethyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 129 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.59 (3H, s), 4.65 (2H, s), 6.97 (1H, d, J= 8.4 Hz), 7.23 (1H, d, J = 8.4 Hz), 7.26 (1H, d, J = 7.6 Hz), 7.74 (1H, dd, J = 2.0, 7.6 Hz), 8.34 (1H, s), 8.54 (1H, d, J = 2.0 Hz).

ESI-MS (m/e) = 459 $(M+H)^+$.

Production Example 130



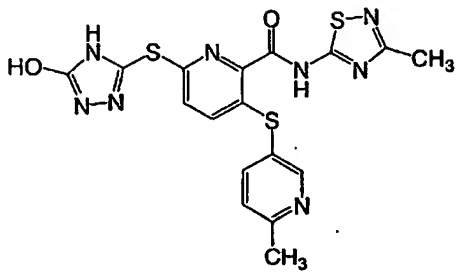
Preparation of 3-[4-(2-hydroxyethyl)-phenyl sulphanyl]-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 130 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-hydroxyethyl-thiophenol and 3-mercapto-4-methyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.61 (3H, s), 2.93 (2H, t, J = 6.4 Hz), 3.72 (3H, s), 3.92 (2H, t, J = 6.4 Hz), 7.06 (1H, d, J = 8.4 Hz), 7.11 (1H, d, J = 8.4 Hz), 7.35 (2H, d, J = 8.0 Hz), 7.47 (2H, d, J = 8.0 Hz), 8.38 (1H, s).

ESI-MS (m/e) = 486 $(M+H)^+$.

Production Example 131

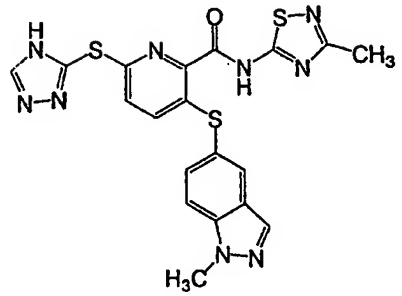


Preparation of 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 131 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-thiadiazole, 3-mercapto-6-methyl-pyridine and 5-hydroxy-3-mercapto-1,2,4-triazole.

^{1}H-NMR (DMSO-d_6) δ = 2.53 (3H, s), 2.65(3H, s), 7.13-7.71 (3H, m), 7.84-7.98 (1H, m), 8.43-8.63 (1H, m).
ESI-MS (m/e) = 459 $(M+H)^+$.

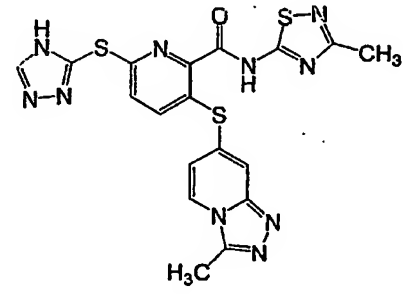
Production Example 132



Preparation of 3-(1-methyl-1H-indazol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 132 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-mercapto-1,2,4-thiadiazole, 5-mercapto-1-methyl-1H-indazole and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 2.53 (3H, s), 4.03 (3H, s), 6.87 (1H, d, J = 8.8 Hz), 7.06 (1H, d, J = 8.8 Hz), 7.39-7.45 (2H, m), 7.94 (2H, m), 8.27 (1H, s).
ESI-MS (m/e) = 482 (M+H) +.

Production Example 133



Preparation of 3-(3-methyl-[1,2,4]-triazolo-[4,3-a]-pyridin-7-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

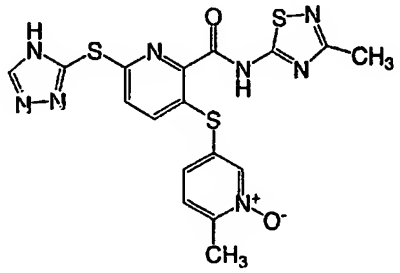
The compound of Production Example 133 can be produced using the same process as in Production

Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-mercapto-1,2,4-thiadiazole, 7-mercapto-3-methyl-[1,2,4]-triazolo- [4,3-a]-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR (DMSO-d_6) δ : 2.49 (3H, s), 2.67 (3H, s), 6.82-6.87 (1H, m), 7.19 (1H, d, J = 8.8 Hz), 7.57 (1H, d, J = 8.8 Hz), 7.86 (1H, s), 8.35 (1H, d, J = 7.2 Hz), 8.70-8.90 (1H, brs).

ESI-MS (m/e) = 483 (M+H) +.

Production Example 134



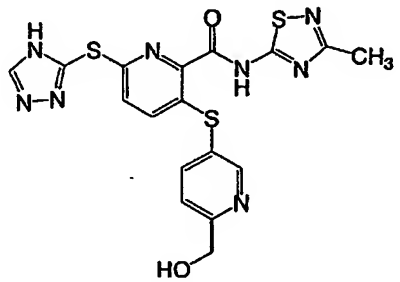
Preparation of 3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 134 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-thiadiazole, 3-mercapto-6-methyl-1-oxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.58 (3H, s), 2.61 (3H, s), 7.16 (1H, d, J = 8.4 Hz), 7.32 (1H, d, J = 8.4 Hz), 7.40-7.45 (2H, m), 8.38 (1H, s), 8.43 (1H, brs).

ESI-MS (m/e) = 459 $(M+H)^+$.

Production Example 135



Preparation of 3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-

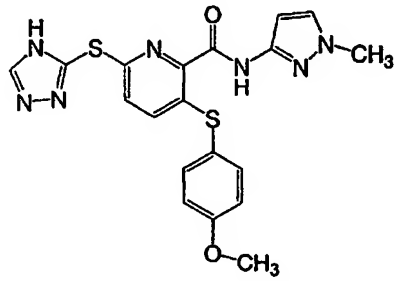
methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 135 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-thiadiazole, 6-hydroxymethyl-3-mercapto-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.62 (3H, s), 4.80 (2H, s), 7.01 (1H, d, J = 8.8 Hz), 7.26 (1H, d, J = 8.8 Hz), 7.56 (1H, d, J = 8.0 Hz), 7.91 (1H, dd, J = 8.0Hz, 1.2 Hz), 8.36 (1H, s), 8.65 (1H, d, J = 1.2 Hz).

ESI-MS (m/e) = 459 (M+H).

Production Example 136



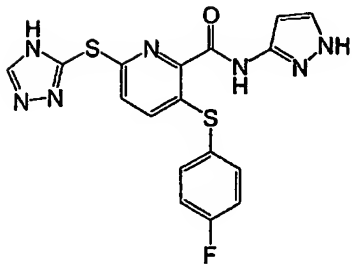
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 136 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.82 (3H, s), 3.83 (3H, s), 6.80 (1H, d, J = 2.4 Hz), 6.93 (1H, d, J = 8.4 Hz), 6.94 (2H, d, J = 8.8 Hz), 7.08 (1H, d, J = 8.4 Hz), 7.25 (1H, d, J = 2.4 Hz), 7.43 (2H, d, J = 8.8 Hz), 8.32 (1H, s).

ESI-MS (m/e) = 440 $(M+H)^+$.

Production Example 137



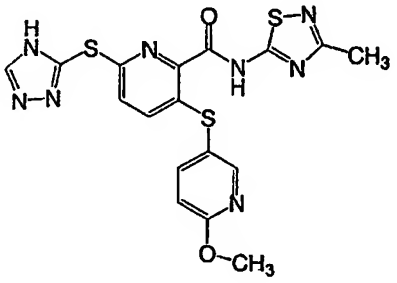
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 137 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1H-[1,2] pyrazole, 4-fluoro thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.87 (1H, bs), 6.94 (1H, d, J = 8.4 Hz), 7.12-7.18 (3H, m), 7.45-7.53 (3H, m), 8.30 (1H, s)

ESI-MS (m/e) = 414 $(M+H)^+$.

Production Example 138



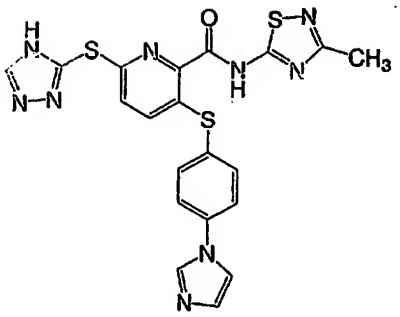
Preparation of 3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 138 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-thiadiazole, 3-mercapto-6-methoxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.63 (3H, s), 4.00 (3H, s), 6.88 (1H, d, J = 8.7 Hz), 7.07 (1H, d, J = 8.7 Hz), 7.29 (1H, d, J = 8.7 Hz), 7.70 (1H, dd, J = 8.7, 2.1 Hz), 8.31-8.40 (2H, m).

ESI-MS (m/e) = 459 $(M+H)^+$.

Production Example 139



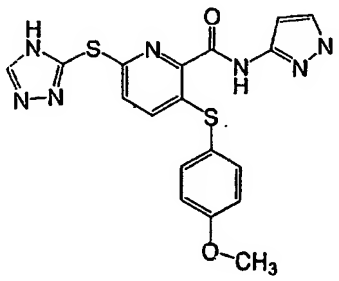
Preparation of 3-[4-(1H-imidazole-1 yl)]-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridinecarboxamide

The compound of Production Example 139 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 5-amino-3-methyl-1,2,4-thiadiazole, 4-(1H-imidazol-1-yl) thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.57 (3H, s), 7.03 (1H, d, J = 8.8 Hz), 7.16 (2H, brs), 7.31 (1H, brs), 7.48 (1H, d, J = 8.4 Hz), 7.65 (2H, d, J = 8.4 Hz), 7.92 (1H, s), 8.32 (1H, s).

ESI-MS (m/e) = 494 $(M+H)^+$.

Production Example 140

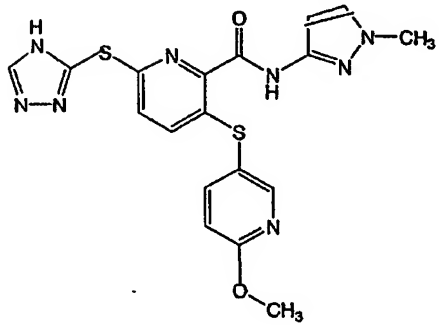


Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 140 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1H-[1,2]-pyrazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 6.86 (1H, d, J = 2.6 Hz), 6.98 (2H, d, J = 8.8 Hz), 6.99 (1H, d, J = 8.8 Hz), 7.17 (1H, d, J = 8.8 Hz), 7.47 (2H, d, J = 8.8 Hz), 7.50 (1H, d, J = 2.6 Hz), 8.34 (1H, s).
ESI-MS (m/e) = 426 $(M+H)^+$.

Production Example 141

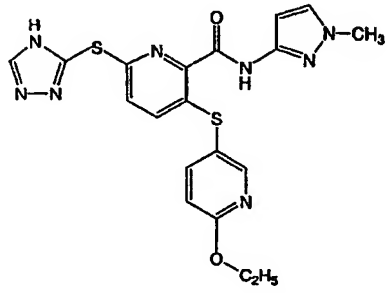


Preparation of 3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 141 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using .3, 6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-pyrazole, 3-mercapto-6-methoxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.81 (3H, s), 3.95 (3H, s), 6.76 (1H, d, J = 2.4 Hz), 6.80 (1H, d, J = 8.4 Hz), 6.93 (1H, d, J = 8.4 Hz), 7.10 (1H, d, J = 8.4 Hz), 7.25 (1H, d, J = 2.4 Hz), 7.65 (1H, dd, J = 8.4Hz, 2.0 Hz), 8.28 (1H, d, J = 2.0 Hz), 8.36 (1H, s), 10.11 (1H, s).
ESI-MS (m/e) = 441 (M+H).

Production Example 142



Preparation of 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-

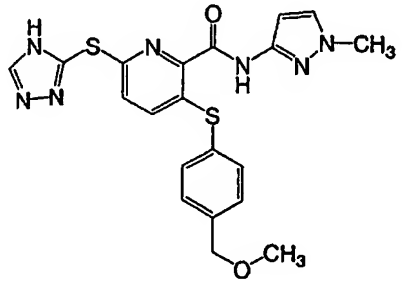
1H-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 142 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using .3, 6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-pyrazole, 3-mercapto-6-ethoxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.43 (3H, t, J = 6.9 Hz), 3.87 (3H, s), 4.42 (2H, q, J = 6.9 Hz), 6.83 (1H, d, J = 8.7 Hz), 6.93 (1H, d, J = 2.1 Hz), 7.02 (1H, d, J = 8.7 Hz), 7.22 (1H, d, J = 8.7 Hz), 7.32 (1H, d, J = 2.1 Hz), 7.69 (1H, dd, J = 8.7, 2.4 Hz), 8.25-8.39 (2H, m).

ESI-MS (m/e) = 455 $(M+H)^+$.

Production Example 143



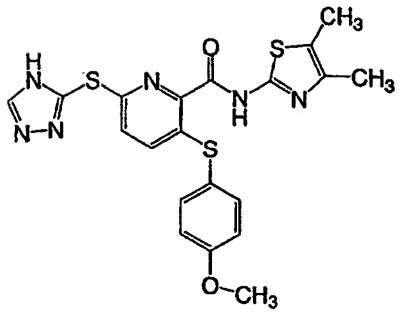
Preparation of 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 143 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using .3, 6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-pyrazole, 4-methoxymethyl-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.45 (3H, s), 3.82 (3H, s), 4.49 (2H, s), 6.83 (1H, d, J = 2.0 Hz), 6.96 (1H, d, J = 8.8 Hz), 7.09 (2H, d, J = 8.8 Hz), 7.25 (1H, d, J = 2.0 Hz), 7.40 (2H, d, J = 7.6 Hz), 7.51 (2H, d, J = 7.6 Hz), 8.31 (1H, s), 10.14 (1H, s).

ESI-MS (m/e) = 440 $(M+H)^+$.

Production Example 144



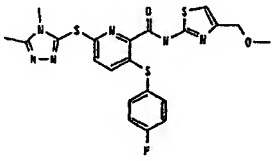
Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4,5-dimethyl thiazol-2-yl)-2-pyridinecarboxamide.

The compound of Production Example 144 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4,5-dimethyl-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.29 (3H, s), 2.33 (3H, s), 3.87 (3H, s), 6.98-7.03 (3H m), 7.21 (1H, d, J = 8.6 Hz), 7.48 (2H, d, J = 8.6 Hz), 8.29 (1H, s).

ESI/MS (m/e) = 471 $(M+H)^+$.

Production Example 145



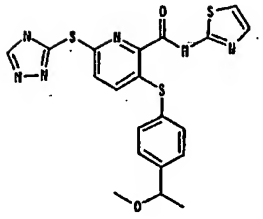
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4,5-dimethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 145 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-methoxymethyl-thiazole, 4-fluoro-thiophenol and 3-mercapto-4,5-dimethyl-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.60 (3H, s), 3.47 (3H, s), 3.62 (3H, s), 4.50 (2H, s), 6.93 (1H, s), 6.98 (1H, d, J = 8.8 Hz), 7.07 (1H, d, J = 8.8 Hz), 7.16 (2H, dd, J = 8.8, 8.8 Hz), 7.53 (2H, dd, J = 5.2, 8.8H).

ESI-MS (m/e) = 503 $(M+H)^+$).

Production Example 146



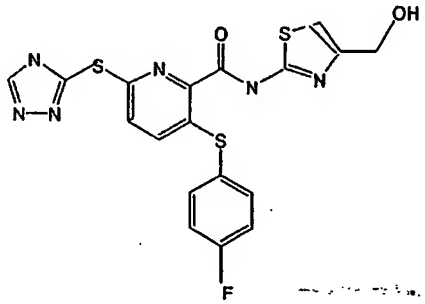
Preparation of 3-(4-[1-methoxyethyl]-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 146 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-(1-methoxyethyl)-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.27 (3H, d, J = 6.4 Hz), 3.30 (3H, s), 4.36 (1H, d, J = 6.4 Hz), 7.03 (1H, d, J = 3.6 Hz), 7.05 (1H, d, J = 8.8 Hz), 7.23 (1H, d, J = 8.8 Hz), 7.41 (2H, d, J = 8.0 Hz), 7.47 (1H, d, J = 3.6 Hz), 7.54 (2H, d, J = 8.0 Hz), 8.35 (1H, s).

ESI-MS (m/e) = 471 $(M+H)^+$.

Production Example 147



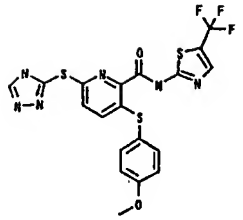
Preparation of 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4) triazol-3-yl-sulphanyl)-N-(4-hydroxymethyl-thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 147 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-hydroxymethyl-thiazole, 4-fluoro-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 4.60 (2H, s), 6.84 (1H, s), 6.93 (1H, d, J = 8.8 Hz), 7.06-7.16 (3H, m), 7.40-7.60

(2H, m), 8.31 (1H, s).
ESI-MS (m/e) = 461 $(M+H)^+$.

Production Example 148

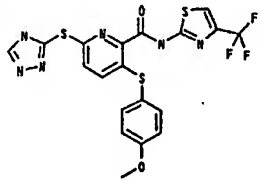


Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-trifluoromethyl thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 148 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-5-trifluoromethyl-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.86 (3H, s), 6.97-7.05 (3H, m), 7.22-7.27 (1H, m), 7.47 (2H, d, J = 8.8 Hz), 7.80 (1H, s), 8.39 (1H, s).
ESI-MS (m/e) = 509 (M-H)-.

Production Example 149



Preparation of 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-trifluoromethyl thiazol-2-yl)-2-pyridinecarboxamide

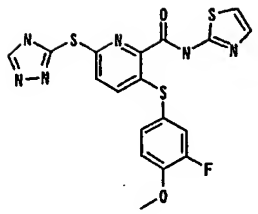
The compound of Production Example 149 is produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-4-trifluoromethyl-thiazole, 4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.85 (3H, s), 6.96-7.00 (3H, m), 7.17 (1H, d, J = 8.0 Hz), 7.44-7.47 (3H, m), 8.37

(1H, s)

ESI-MS(m/e) = 511 $(M+H)^+$.

Production Example 150



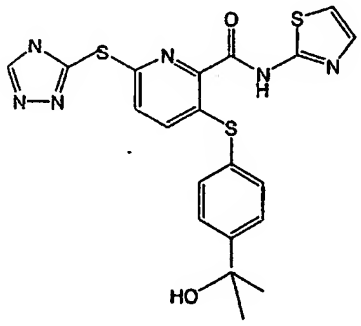
Preparation of 3-(3-fluoro-4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

The compound of Production Example 150 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 3-fluoro-4-methoxy-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.95 (3H, s), 7.01-7.06 (3H, m), 7.23-7.32 (3H, m), 7.47 (1H, d, J = 4.0 Hz), 8.32 (1H, s).

ESI-MS (m/e) = 461 (M+H).

Production Example 151



Preparation of 3-[4-(1,1-dimethyl-1-hydroxymethyl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridinecarboxamide

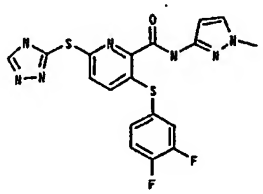
The compound of Production Example 151 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-

dichloro-2-pyridinecarboxylic acid, 2-amino-thiazole, 4-(1,1-dimethyl-1-hydroxymethyl)-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 1.63 (6H, s), 6.99-7.03 (2H, m), 7.18 (1H, d, J = 8.4 Hz), 7.39 (1H, d, J = 3.6 Hz), 7.51 (2H, d, J = 8.4 Hz), 7.58 (2H, d, J = 8.4 Hz), 8.30 (1H, s).

ESI-MS (m/e) = 471 $(M+H)^+$.

Production Example 152



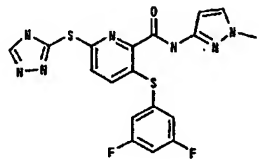
Preparation of 3-(3,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 152 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 3,4-difluoro-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.84 (3H, s), 6.82 (1H, d, J = 2.0 Hz), 6.94 (1H, d, J = 8.8 Hz), 7.15 (1H, d, J = 8.8 Hz), 7.20-7.41 (4H, m), 8.33 (1H, s).

ESI-MS (m/e) = 446 $(M+H)^+$.

Production Example 153

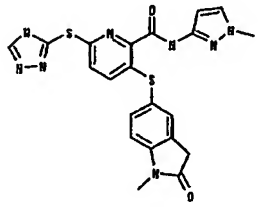


Preparation of 3-(3,5-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 153 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 3,5-difluoro-thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.81 (3H, s), 6.81 (1H, d, J = 2.8Hz), 6.83-6.90 (1H, m), 7.04-7.06 (2H, m), 7.16 (1H, d, J = 8.8 Hz), 7.27 (1H, d, J = 2.8 Hz), 8.27 (1H, s).
ESI-MS (m/e) = 446 $(M+H)^+$.

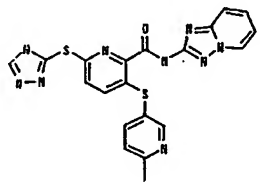
Production Example 154



Preparation of 3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 154 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 5-mercapto-1-methyl-1,3-dihydroindole-2-one and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 3.15 (3H, s), 3.48 (2H, s), 3.76 (3H, s), 6.75 (1H, d, J = 2.4 Hz), 6.83 (1H, d, J = 8.0 Hz), 6.88 (1H, d, J = 8.8 Hz), 7.02 (1H, d, J = 8.8 Hz), 7,23 (1H, d, J = 2.4 Hz), 7.31 (1H, d, J = 1.6 Hz), 7.41 (1H, dd, J = 8.0, 1.6 Hz), 8.22 (1H, s).
ESI-MS (m/e) = 479 $(M+H)^+$.

Production Example 155

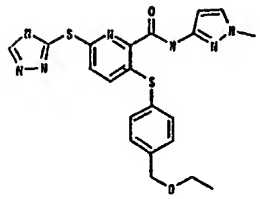


Preparation of 3-(6-methyl-pyridine-3-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazolopyridine-2-yl)-2-pyridinecarboxamide

The compound of Production Example 155 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 2-amino-[1,2,4] triazolopyridine, 3-mercapto-6-methyl-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 2.58 (3H, s), 6.93 (1H, d, J = 8.8 Hz), 7.01 (1H, t, J = 6.4 Hz), 7.16 (1H, d, J = 8.8 Hz), 7.24 (1H, d, J = 8.0 Hz), 7.51-7.60 (2H, m), 7.73 (1H, dd, J = 8.0, 2.4 Hz), 8.32 (1H, s), 8.53 (1H, s), 8.60 (1H, d, J = 6.4 Hz).
ESI-MS (m/e) = 462 $(M+H)^+$.

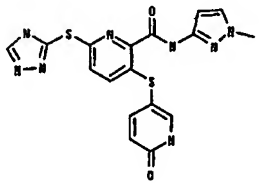
Production Example 156



Preparation of 3-(4-ethoxy methyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 156 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 4-ethoxymethyl-thiophenol and 3-mercapto-1,2,4-triazole.
^{1}H-NMR ($CDCl_3$) δ : 1.28 (3H, t, J = 6.8 Hz), 3.60 (2H, q, J = 6.8 Hz), 3.83 (3H, s), 4.54 (2H, s), 6.85 (1H, d, J = 2.0 Hz), 6.98 (1H, d, J = 8.8 Hz), 7.10 (1H, d, J = 8.8 Hz), 7.26 (1H, d, J = 2.0 Hz), 7.41 (2H, d, J = 8.0 Hz), 7.51 (2H, d, J = 8.0 Hz), 8.31 (1H, s).
ESI-MS (m/e) = 468 $(M+H)^+$.

Production Example 157



Preparation of 3-(6-oxo-1,6-dihydro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

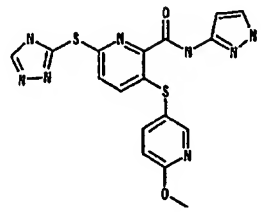
The compound of Production Example 157 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 3-mercapto-6-methoxy-

pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.86 (3H, s), 6.63 (1H, d, J = 9.3 Hz), 6.85 (1H, d, J = 2.1 Hz), 7.21 (1H, d, J = 9.0 Hz), 7.27 (1H, d, J = 9.0 Hz), 7.33 (1H, m), 7.45 (1H, brd, J = 9.3 Hz), 7.58 (1H, d, J = 2.1 Hz), 8.35 (1H, s).

ESI-MS (m/e) = 427 $(M+H)^+$.

Production Example 158



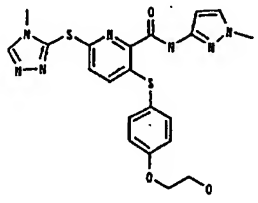
Preparation of 3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 158 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 3-mercapto-6-methoxy-pyridine and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$ δ = 4.00 (3H, s), 6.84-6.94 (2H, m), 7.02 (1H, d, J = 9.0 Hz), 7.22 (1H, d, J = 9.0 Hz), 7.52 (1H, m), 7.70 (1H, m), 8.31-8.40 (2H, m).

ESI-MS (m/e) = 427 $(M+H)^+$.

Production Example 159



Preparation of 3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,41 triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,21-pyrazol-3-yl)-2-pyridinecarboxamide

The compound of Production Example 158 can be produced using the same process as in Production Example 1, a process based on this or a combination of these with conventional procedures, using 3,6-dichloro-2-pyridinecarboxylic acid, 3-amino-1-methyl-1H-[1,2] pyrazole, 4-hydroxyethyl oxy-

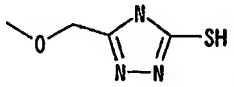
thiophenol and 3-mercapto-1,2,4-triazole.

^{1}H-NMR ($CDCl_3$) δ : 3.73 (3H, s), 3.85 (3H, s), 4.00 (2H, m), 4.13 (2H, m), 6.87 (1H, d, J = 2.1 Hz), 6.95-7.06 (3H m), 7.34-7.31 (2H, m), 7.46 (2H, d, J = 8.7 Hz), 8.41 (1H, s).

ESI-MS (m/e)= 484[M+H]+.

Below a process for the production of the compound used in preparation of the compound in accordance with this invention is described as Reference Example 1-6.

Reference Example 1



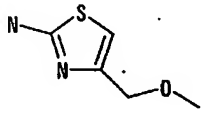
Preparation of 5-methoxymethyl-3-mercapto-1,2,4-triazole

Methoxyacetyl chloride 2.82 g (0.023 mole) were added to pyridine solution (15 ml) of thiosemicarbazide 2.09 g (0.0230 mole) and stirred at room temperature twenty-four hours. The reaction solution was concentrated, and methanol (10 ml), methanol solution (8 ml) of sodium methoxide of 25 wt.% were added, and it was heated under reflux twenty-four hours. It was cooled to room temperature, and next the solvent was eliminated by distillation, and concentrated hydrochloric acid was added, and it was acidified. The precipitated solid was washed with distilled water after filtration, and it was dried, and the title compound 1.0 g (yield 33 %) was obtained.

^{1}H-NMR (DMSO) δ = 3.24 (3H, s), 4.29 (2H, s).

ESI-MS (m/e) = 146 $(M+H)^+$.

Reference Example 2



Preparation of 2-amino-4-methoxymethylthiazole

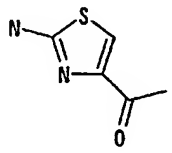
Thiourea 8.06 g (106 mmol) was added to dimethoxyethane solution (120 ml) of dichloroacetone 13.4 g (106 mmol) and was stirred at 55°C for three hours. The reaction liquor was concentrated, and methanol (200 ml) and magnesium sulfate 15.1 g (125 mmol) were added to the obtained white solid, and the mixture was heated under reflux for three days. The reaction mixture was filtered with cellite, and the filtrate was concentrated, and thereafter it was partitioned with chloroform and saturated aqueous sodium bicarbonate solution. The organic layer was dried, and, after concentration, title

compound 6.59 g (yield = 43 %) was obtained as yellow solid by refining the obtained residue by crystallization, and silica gel column chromatography (ethyl acetate) and mixed solvent of hexane-acetic acid ethyl ester (4 : 1).

^{1}H-NMR ($CDCl_3$) d : 3.44 (3H, s), 4.34 (2H, s), 6.45 (1H, s).

ESI-MS (m/e) = 145 $(M+H)^+$.

Reference Example 3



Preparation of 4-acetyl-2-aminothiazole

N,O-dimethyl hydroxyamine hydrochloride 660 mg (6.77 mmol), triethylamine 1.40 ml (9.96 mmol), N-hydroxybenzotriazole hydrate 1.10 g (8.14 mmol) and 1-(3-dimethylaminopropyl)-3-ethyl carbodiimide hydrochloride 1.60 g (8.35 mmol) were added successively to N,N-dimethylformamide solution (30 ml) of 2-(tert-butyloxycarbonyl amino)-4-carboxy thiazole 1.30 g (5.14 mmol), and thereafter, it was stirred at room temperature for five days. The reaction liquor was concentrated, and ethyl acetate was added to the residue, and it was washed with 1N hydrochloric acid aqueous solution water, and saturated sodium chloride aqueous solution, dried, and concentrated under reduced pressure, and amide compound 1.35 g (yield = 91 %) was obtained as an oily substance.

Tetrahydrofuran solution (40 ml) of the obtained amide compound 920 mg (3.20 mmol) was cooled in 78 degrees, and methyl lithium diethyl ether solution 18.0 ml (18.0 mmol) was added, and the mixture was stirred for seven hours. Ammonium chloride saturated aqueous solution was added to the reaction liquid and the liquid extracted with ethyl acetate. The organic layer was washed with water, and thereafter, it was dried, and it was concentrated, and the acetyl compound 666 mg (yield = 86 %) was obtained as an oily substance.

Trifluoroacetic acid 5 ml was added to chloroform solution (10 ml) of the obtained acetyl compound, and it was stirred at room temperature for one hour and a half. The reaction liquor was concentrated, and it was neutralized with saturated aqueous sodium bicarbonate solution, and it was separated by filtration, and the title compound 149 mg (yield = 59 %) was obtained as a white solid.

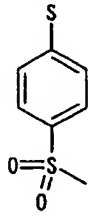
^{1}H-NMR ($CDCl_3$) δ : 2.48 (3H, s), 7.35 (1H, s).

ESI-MS (m/e) = 143 $(M+H)^+$.

Reference Example 4

Preparation of 4-methylsulfonyl benzene thiol

(The source text has a major editing error which has been corrected)



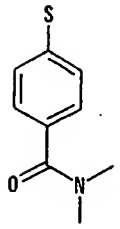
35 % aqueous hydrogen peroxide 18 ml and methyl trioxo rhenium 180 mg (0.72 mmol) were added to chloroform solution (150 ml) of 4-methylthio phenol 5.0 g (36 mmol), under ice cooling, and thereafter, it was stirred at room temperature for 30 minutes. Manganese dioxide was added under ice cooling to the reaction liquor and was stirred at room temperature for four hours, and thereafter, saturated aqueous sodium chloride solution was added, and extraction with chloroform was carried out. The organic layer was washed with saturated aqueous sodium chloride solution, and thereafter, it was dried, and it was concentrated, and 4-methylsulphonylphenol 5.0 g (yield = 81 %) was obtained as a white solid.

1,4-diazabicyclo[2.2.2] octane 6.5 g (58 mmol) and dimethyl thiocarbamoyl chloride 5.4 g (44 mmol) were added to N,N-dimethylformamide solution (100 ml) of the obtained 4-methylsulfonyl phenol 5.0 g (29 mmol), and thereafter, were stirred at 75°C for four hours. Water was added to the reaction liquid and the liquid extracted with ethyl acetate, and the organic layer was washed with water, saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution. After drying and concentrating, the obtained residue was recrystallised from mixed solvent of hexane-chloroform, and O-4-methylsulfonyl phenyl dimethyl thio carbamate 4.8 g (yield = 63 %) was obtained as white solid.

The obtained O-4-methylsulfonyl phenyl dimethyl thio carbamate 4.8 g (18 mmol) was stirred at 180°C for ten hours, and it was returned to room temperature, and thereafter, methanol 10 ml were added. 2N-sodium hydroxide aqueous solution (10 ml) was added to the reaction solution thereof and was heated under reflux for eight hours 30 minutes. 1N hydrochloric acid aqueous solution was added to the reaction solution, extraction was carried out with ethyl acetate, and the organic layer was washed with saturated aqueous sodium chloride solution. The residue obtained after drying and concentration was refined using silica gel column chromatography (hexane : ethyl acetate = 2:1-chloroform: methanol = 10:1) and the title compound 3.6 g (yield = 100 %) was obtained as white solid.

^{1}H-NMR ($CDCl_3$) d : 3.04 (3H, s), 3.69 (1H, s), 7.63 (2H, d, J = 7.6 Hz), 7.87 (2H, d, J = 7.6 Hz).

Reference Example 5



Preparation of 4-dimethylcarbamoyl benzene thiol

Carbonyldiimidazole 1.50 g (6.77 mmol) and tetrahydrofuran solution 4.70 ml (8.35 mmol) of dimethylamine were added successively to tetrahydrofuran solution (50 ml) of 4-methylthio benzoic acid 1.30 g (5.14 mmol), and thereafter, it was stirred at room temperature for two hours and a half. Acetic acid ethyl ester was added to the reaction solution and it was washed with 1N hydrochloric acid aqueous solution, water and saturated aqueous sodium chloride solution. The organic layer was dried, and it was concentrated, and amide compound 960 mg of crude product was obtained as an oily substance.

3-chloroperbenzoic acid 980 mg (4.90 mmol) was added slowly at room temperature to chloroform solution (50 ml) of the obtained amide compound, and it was stirred for one hour. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction solution and it was stirred for 30 minutes, and thereafter, it was extracted with ethyl acetate, and the organic layer was washed with water and saturated aqueous sodium chloride solution. It was dried, and it was concentrated, and sulfoxide compound 910 mg of crude product was obtained as an oily substance.

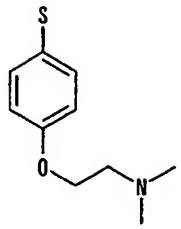
2,6-lutidine 1.56 ml (13.4 mmol) and trifluoroacetic acid anhydride 1.80 ml (12.9 mmol) were added successively to a chloroform solution (20 ml) of the obtained sulfoxide compound, and it was stirred at room temperature for one hour. The reaction solution was concentrated, and triethylamine 5 ml and methanol 5 ml were added and the mixture was stirred for 30 minutes. The reaction solution was concentrated, and diethyl ether was added to the obtained residue and was washed with 1N hydrochloric acid aqueous solution, saturated aqueous sodium bicarbonate solution. The organic layer was dried, and it was concentrated, and the title compound 487 mg (yield = 62 %) was obtained as an orange oil.

Wherein, it was used in the next reaction without refining the obtained crude product.

^{1}H-NMR ($CDCl_3$) δ : 3.03 (3H, s), 3.14 (3H, s), 7.22-7.38 (3H, m), 7.46-7.52 (1H, m).

ESI-MS (m/e) = 182[M+H]+.

Reference Example 6



Preparation of 4-dimethylaminoethyl oxy-benzene thiol

Dimethylaminoethyl chloride hydrochloride 2.40 g (17.1 mmol) and potassium carbonate 5.83 g (42.2 mmol) were added successively to N,N-dimethylformamide solution (70 ml) of 4-iodophenol 3.00 g (13.6 mmol), and were stirred at 70°C for 15 hours. The reaction liquor was diluted with water and extraction was carried out with ethyl acetate. The organic layer was washed with water and saturated aqueous sodium chloride solution, and thereafter, it was dried, and it was concentrated. By refining the obtained residue with silica gel column chromatography (chloroform : methanol = 30 : 1), iodo derivative 840 mg (yield = 21 %) was obtained as oily substance. Ethylene glycol 120 μl (2.15 mmol), potassium carbonate 305 mg (2.21 mmol), 4-methoxy-α toluene thiol 150 μl (1.08 mmol) and copper iodide 20 mg (0.105 mmol) were added to 2-propanol solution (8 ml) of the obtained iodo derivative 317mg (1.08 mmol), and the reaction liquor was heated under reflux for 40 hours. The reaction liquor was filtered with celite, and thereafter, filtrate was partitioned with chloroform and saturated aqueous sodium chloride solution. The organic layer was dried, and concentrated under reduced pressure, and anisole (180 microlitres) and trifluoroacetic acid (1.5 ml) were added to successively to the obtained oily substance 298 mg, and thereafter, it was stirred at 70°C for two hours. The reaction liquor was concentrated and was used in the next reaction without refining the obtained crude product.

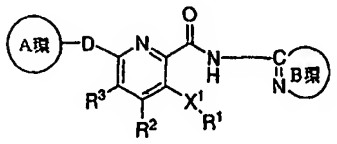
ESI-MS (m/e) = 198 $(M+H)^+$.

Possible Applications in Industry

Novel 2-pyridinecarboxamide derivative represented by formula (1) in accordance with this invention is useful in therapy and/or prevention of obesity or diabetes mellitus and diabetes mellitus complication in a sphere of drug by showing excellent glucokinase activity.

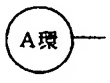
Patent Claims

1. A compound represented by formula (1) or pharmacologically acceptable salts thereof

ring A  ring B

(I)

[wherein, X1 denotes N, S or O, or divalent saturated hydrocarbon group of carbon number 1-6 (when carbon number of said divalent saturated hydrocarbon group is 2 or more, one of carbon atom in said divalent saturated hydrocarbon group may be substituted by nitrogen atom, oxygen atom or sulfur atom), R1 denotes 6-10 membered aryl group, 5-10 membered heteroaryl group, cycloalkyl group of carbon number 3-7 or lower alkyl group {the said R1 may have, on R1, one or two groups selected from the group comprising amino group, lower alkyl group (hydrogen atom of lower alkyl group may be substituted by hydroxy group, lower alkoxy group, halogen atom, carbamoyl group, mono or di-lower alkyl carbamoyl group, carboxyl group, alkoxy carbonyl group, alkanoyl group, amino group or mono or di-lower alkyl amino group), lower alkoxy group (hydrogen atom of methyl group or methylene group composing said lower alkoxy group may be substituted by hydroxy group, halogen atom, carbamoyl group, mono or di-lower alkyl carbamoyl group, carboxyl group, alkoxycarbonyl group, alkanoyl group, amino group or mono or di-lower alkyl amino group), carbamoyl group, lower alkyl carbamoyl group, dilower alkyl carbamoyl group, carbamoyl amino group, carbamoyloxy group, carboxyl group, cyano group, sulphamoyl group, trifluoromethyl groiup, halogen atom, hydroxy group, formyl group, C2-C6-alkanoyl group, N-C2-C6-alkanoyl amino group, C1-C6-alkylthio group, N-C1-C6-alkyl sulphamoyl group, N,N-di-C1-C6-alkyl sulphamoyl group, C1-C6-alkyl sulphinyl group, C1-C6-alkylsulfonyl group, N-C1-C6-alkylsulfonyl amino group, C1-C6-alkoxycarbonyl group, N-C1-6 alkylamino group and N,N-di-C1-C6-alkylamino group}, D denotes O or S, R2 and R3 may be the same or different and denote hydrogen atom, lower alkyl group, lower alkoxy group, halogen atom, formula (II)

ring A 

(II)

shows 5-7 membered heteroaryl group or 6-10 membered aryl group which may have on the said ring, 1 or 2 group selected from the group comprising lower alkyl group, lower alkoxy group, trifluoromethyl group, hydroxy group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group) and halogen atom, and formula (III)

ring B

(III)

shows monocyclic or polycyclic heteroaryl group wherein carbon atom in the said ring bonded to nitrogen atom of the amide group contained in formula (1) forms C=N with nitrogen atom in the said ring {the said heteroaryl group may have in B ring, 1 or 2 substituent selected from the group comprising lower alkyl group, lower alkoxy group, halogen atom, trifluoromethyl group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group), amino (the said amino group may be substituted by lower alkyl group), alkanoyl group, carboxyl group, alkoxycarbonyl group and cyano group}].

2. A compound in accordance with Claim 1, wherein D is S.

3. A compound in accordance with any of Claim 1 or 2, wherein R2 and R3 are both hydrogen atoms.

4. A compound in accordance with any of Claims 1-3, wherein A ring is phenyl group, isothiazolyl group, imidazolyl group, oxazolyl group, thiadiazolyl group, thienyl group, triazolyl group, tetrazolyl group, pyridyl group, pyrimidinyl group, furyl group, thiazolyl group, isoxazolyl group or pyrazolyl group that which may have 1 or 2 group selected from the group comprising lower alkyl group, lower alkoxy group, trifluoromethyl group, hydroxy group, hydroxyalkyl group (hydrogen atom of hydroxy group in the said hydroxyalkyl group may be further substituted by lower alkyl group) and halogen atom on the said ring.

5. A compound in accordance with any of Claims 1-4, wherein X1 is a group selected from the group comprising nitrogen atom, sulfur atom, oxygen atom, -CH2-, -N-CH2-, -S-CH2-, -O-CH2-, -CH2-N-, -CH2-O- and -CH2-S-.

6. A compound in accordance with any of Claims 1-5, wherein B ring is 5-6 membered heteroaryl group having at least one nitrogen atom of C=N composing said ring as heteroatom of said ring or 9-10 membered heteroaryl group in which said heteroaryl group and phenyl group or pyridyl group are condensed.

7. A compound in accordance with any of Claims 1 to 6, wherein R1 is 6-10 membered aryl group, 5-10 membered heteroaryl group or cycloalkyl group of carbon number 3-7.

8. A compound in accordance with any of Claims 1 to 6, wherein R1 is 6-10 membered aryl group or 5-10 membered heteroaryl group.

9. A compound in accordance with any of Claims 1-6, wherein R1 is 6-10 membered aryl group.

10. A compound in accordance with any of Claims 1-6, wherein R1 is 5-10 membered heteroaryl group.

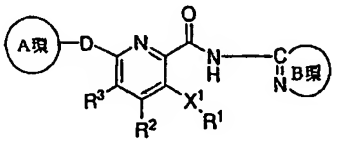
11. A compound in accordance with Claim 9 or 10, wherein substituent of A ring is hydrogen atom, lower alkyl group, lower alkoxy group, hydroxy group or hydroxy lower alkyl group (hydrogen atom of hydroxy group in hydroxy lower alkyl group may be further substituted by lower alkyl group).

12. A compound in accordance with any of Claims 9 to 11, wherein B ring is thiazolyl group, imidazolyl group, isothiazolyl group, thiadiazolyl group, triazolyl group, oxazolyl group, isoxazolyl group, pyrazinyl group, pyridyl group, pyridazinyl group, pyrazolyl group, pyrimidinyl group, pyrido thiazolyl group or benzothiazolyl group.

13. A compound in accordance with any of Claims 1-10, wherein substituent of B ring is hydrogen atom, lower alkyl group, halogen atom, hydroxyalkyl group, amino alkyl group or alkanoyl group.

14. A compound in accordance with any of Claims 9 to 12, wherein substituent of R1 is hydrogen atom, hydroxyalkyl group, lower alkyl group, lower alkoxy group, carbamoyl group, alkylcarbamoyl group, dialkyl carbamoyl group, cyano group, trifluoromethyl group, halogen atom, 2-6C alkanoyl group, N-C2-C6 alkanoyl amino group, C1-C6- alkylsulfonyl group, C1-C6- alkylamino group or amino alkyl group.

15. A compound in accordance with any of Claims 1 to 14 or pharmacologically acceptable salts thereof, wherein the compound represented by aforesaid formula (1)

ring A  ring B

(I)

(each symbol has the same the aforesaid definitions) is
3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-imidazol-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyl sulphanyl)-6-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(thiazol-2-yl-sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,
3-(2-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-phenyl sulphanyl-6-(4H-[1,2,4]-triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(4-fluoro-phenyloxy)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(4-methoxy-phenylmethyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(3-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,
3-(2,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-cyano-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-4-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-acetyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(thiophen-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-chloro-phenyl sulphanyl)-6-(4H-[1,2,41 triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(3H-[1,2,3] triazol-4-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methylsulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazole-3-yl-sulphanyl)-N-(5-hydroxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(5-methoxymethyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-trifluoromethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-dimethylamino methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2- pyridine carboxamide,

3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methyl sulphamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-hydroxy-cyclohexyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridazine-3-yl)-2-pyridine carboxamide,

3-(pyrazine-2-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(1-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4) triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(2-methyl-thiazol-4-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(1-methyl-1H-tetrazol-5-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-phenoxy-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(2-chloro-phenylmethyl-amino)-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis (pyridine-2-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(4-fluoro-phenyl sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(thiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3,6-bis-(5-methyl-[1,3,4] thiadiazol-2-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-methyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(isoxazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,3,4] thiadiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl carbonyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyrimidine-4-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(pyridine-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-ethoxycarbonyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-phenyloxy methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazole-2 yl)-2-pyridine carboxamide,

3-phenyl sulphanyl methyl-6-(4-methyl-4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-phenylmethyl-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro- phenyl methyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminomethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-4-yl)-2-pyridine carboxamide,

3-(4-dimethylcarbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(4-hydroxyethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methoxycarbonyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(pyrimidine-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(1-methyl-pyrrolidine-3-yloxy)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-diethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-pyrrolidino ethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-dimethylaminoethyl oxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(pyrazol-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-carbamoylmethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(5-bromo-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(pyridine-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [5,4-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,5] thiadiazol-3-yl)-2-pyridine carboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methoxy-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-[3-cyclopropyl-[1,2,4]-thiadiazol-5-yl]-2-pyridine carboxamide,

3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2-fluoro-pyridin-4-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(2-methoxy-pyrimidin-5-yl sulphanyl)-6-(2H-[1,2,41 triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-diethylcarbamoyl methyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-cyclopropyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(pyrazol-4-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-dimethylamino sulfonyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(5-fluoro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2,3-dihydro-benzofuran-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazine-3-yl)-2-pyridine carboxamide,

3-(4-carboxy-phenyl sulphanyl)-6-(5-methyl-[1,2,4] triazole-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(2-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(thiazolo [4,5-b] pyridine-2-yl)-2-pyridine carboxamide,

3-(5-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4,4-difluoromethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-hydroxyethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(2-methyl-imidazo-[1,2-a]-pyridin-6-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-hydroxymethyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(2-hydroxyethyl)-phenyl sulphanyl]-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridin-3-yl sulphanyl)-6-(5-hydroxy-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-methyl-1H-indazol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,41-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(3-methyl-[1,2,4]-triazolo-[4,3-a]-pyridin-7-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(1-oxy-6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(6-hydroxymethyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-[4-(1H-imidazol-1-yl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4,5-dimethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4,5-dimethyl-4H-[112,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-(1-methoxyethyl)-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-hydroxymethyl-thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(5-trifluoromethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-trifluoromethyl thiazol-2-yl)-2-pyridine carboxamide,

3-(3-fluoro-4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-[4-(1,1-dimethyl-1-hydroxymethyl)-phenyl sulphanyl]-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide,

3-(3,4-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(3,5-difluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(1-methyl-2-oxo-2,3-dihydro-1H-indol-5-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,

3-(6-methyl-pyridine-3-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] triazolopyridine-2-yl)-2-pyridine carboxamide,
3-(4-ethoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(6-oxo-1,6-dihydro-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide,
3-(4-hydroxyethyl oxy-phenyl sulphanyl)-6-(4-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-[1,2]-pyrazol-3-yl)-2-pyridine carboxamide.

16. The compound which is 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

17. The compound which is 3-(4-fluoro-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

18. The compound which is 3-(4-methoxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methoxymethyl-thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

19. The compound which is 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

20. The compound which is 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

21. The compound which is 3-(hydroxyethyloxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

22. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

23. The compound which is 3-(4-hydroxyethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

24. The compound which is 3-(6-methyl-pyridine-3-yl-sulphanyl)-6-(4H-[1,2,4] triazol-3-yl-sulphanyl)-N-(4-methyl-thiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

25. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

26. The compound which is 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

27. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-([1,2,4] thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

28. The compound which is 3-(4-dimethylaminoethyl oxy-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4] thiadiazol-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

29. The compound which is 3-[4-(2-hydroxyethyl-phenyl sulphanyl)]-6-(5-methyl-4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

30. The compound which is 3-(6-methyl-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

31. The compound which is 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(3-methyl-[1,2,4]-thiadiazol-5-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

32. The compound which is 3-(6-ethoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(pyrazine-2-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

33. The compound which is 3-(6-methoxy-pyridin-3-yl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

34. The compound which is 3-(4-methoxymethyl-phenyl sulphanyl)-6-(4H-[1,2,4] triazol-3-yl sulphanyl)-N-(1-methyl-1H-pyrazol-3-yl)-2-pyridine carboxamide or pharmacologically acceptable salts thereof.

35. Medicinal composition formed from the following (1)-(3) used in order to treat, prevent, and/or delay the onset of type II diabetes

(1) a compound represented by (I);

(2) one or more compounds selected from the group comprising (a)-(g);

(a) Other glucokinase activator.

(b). Bisguanide.

(c). PPAR agonist.

(d). Insulin.

(e). Somatostatin.

(f). α-glucosidase inhibitor.

(g). Secretion promoting agent of insulin.

(3) Pharmacologically acceptable carrier.

36. A glucokinase activator containing as an effective component, the compound in accordance with any of Claims 1 to 34.

37. A diabetes mellitus therapeutic and/or preventive agent, containing as an effective component, the compound in accordance with any of Claims 1 to 34.

38. An obesity therapeutic and/or preventive agent, containing as an effective component, the compound in accordance with any of Claims 1 to 34.

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